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UDC 581.143.6:633.11

Morphogenesis in Tissue Culture of Spring Wheat
18400018 Alma-Ata VESTNIK AKADEMII NAUK KAZAKHSKOY SSR in Russian No 5, May 88 pp 63-68

[Article by S. V. Kushnarenko and I. R. Rakhimbayev]

[Abstract] Callus formation, risogenesis and regeneration processes were studied in tissue cultures of ten brands of soft and four brands of hard spring wheat in relation to a number of factors: genotype, origin and polarity of explantates and composition of nutrient media. The experiments showed that the ability of callus development and regeneration of plants in wheat tissue cultures is related to the genotype. Callus tissues of the soft wheat brands showed greater ability to form sprouts and roots (hemmorisogenesis) than the hard wheat brands. The best explants for obtaining morphogenetic calluses were immature embryos (1.0-1.4 mm) placed in the nutrient medium with the fascicles in upward position. The Murasige-Skug medium was most effective in formation of wheat callus tissue and in development of plants from them. Figures 2; references 11: 3 Russian, 8 Western.

In Vitro and In Vivo Activity of the Ionophore Antibiotic 985-I

18400015b Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 301 No 2, Jul 88 pp 493-495

[Article by A. I. Zebrev, Yu. N. Antonenko, V. G. Voytenko, V. V. Berezhinskaya, G. B. Dolgova, V. B. Nikitin, L. P. Ivanitskaya, and S. M. Navashin, All Union Scientific Research Institute of Antibiotics, Moscow; Moscow State University imeni M. V. Lomonosov]

[Abstract] Animal experiments and experiments on isolated mouse organs were conducted to investigate the aminophoric activity of the pyrrol-ether antibiotic 985-I (with a selectivity of K much greater than C greater than Mg greater than Na) and its effect in various systems. In low concentrations (10^{-7}-10^{-6} M), 985-I exhibited potassium ionophore activity, with the release of K ions from the mitochondria, whose transmembrane potential increased. The effect of the 985-I ionophore was identical to that of the typical nonelectrogenic K^+/H^+ exchanger. The antibiotic also evoked a glucose-dependent inhibition of the secretion of histamine from fat cells activated by the Ca-ionophore A23187 or substance 48/80 and reduced the tonus of isolated smooth muscles of guinea pigs. At higher concentrations, 985-I caused Ca-dependent histamine secretion and degranulation of fat cells. At concentrations higher than 6 X 10^{-5} M, the antibiotic prompted a release of histamine unlike secretion, since the release of the mediator was suppressed in the absence of Ca ions and at 3°C, but not by antiallergy compounds or metabolic inhibitors. Nor was the release intensified by ouabain or glucose. In vitro, 985-I in doses of 10^{-5}-10^{-4} M caused contraction of smooth muscles from isolated fragments of ileum, trachea, and parenchyma of the lungs of a guinea pig and rectus abdominis of a frog. The multifaceted activity of 985-I is associated with its pronounced membranotropic action. The antibiotic can be used as a selective potassium ionophore at low concentrations, a calcium ionophore and aminophore at higher concentrations. Figures 3; references 5: 1 Russian, 4 Western.

UDC 577.17.04,591.48

Synthesis and Secretion of Nerve Growth Factor (NGF) by Salivary Glands of Venomous and Nonvenomous Snakes

18400016c Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 301 No 3, Jul 88 (manuscript received 18 Jan 88) pp 754-756

[Article by V. A. Paalme, U. V. Arumyae, Yu. R. Siygur, T. E. Neuman, S. A. Shepilov, and M. Yu. Saarma, Institute of Chemical and Biological Physics, Estonian SSR Academy of Sciences, Tallin; Central Asian Zoological Center, Tashkent]

[Abstract] An analysis was conducted on the NGF and its precursors isolated from the salivary and venom glands of the viper Vipera lebetina and the racer Elaphe dione. Conventional biochemical techniques combine with immunoblotting with monoclonal antibodies against viper NGF led to the identification of a 32.5 kD NGF in the venom of the viper, and 67 and 69 kD NGF components in the extracts of the salivary and venom glands. The salivary gland of the nonvenomous racer yielded three components reacting with the antibodies: 37, 70, and 72 kD. The extracts from the salivary glands of the viper and the racer demonstrated NGF activities by stimulated axon growth in primed PC-12 cells. Southern hybridization experiments with NGF cDNA showed that in all cases and in both species only a single 2200 bp mRNA was responsible for the precursors, indicating that actual formation of NGF is the result of posttranslational modification. An immunofluorescent assay developed with Eu^+ labeled mono- and polyclonal antibodies showed that the levels of NGF in the venom gland of the viper were on the order of 27 plus or minus 1.9 ng/mg soluble protein, and in the salivary gland on the order of 17 plus or minus 6.7 ng/mg. To date, the functional significance of NGF in the salivary and venom glands remains unclear. Figures 3; references 10: 2 Russian, 8 Western.

Lytic Activity For Gram-Positive Microorganisms of Enzyme Preparation Isolated From Pseudomonas Lytica Culture

18400490A Moscow ANTIBIOTIKI I KHIMIOTERAPIYA in Russian Vol 33 No 4, Apr 88 (manuscript received 22 Oct 86) pp 271-275

[Article by Ye. L. Tauson, A. I. Severin, T. S. Shobukhova, M. V. Lebedeva, Z. M. Andreyeva and I. S. Kulayev, Institute of Biochemistry and Physiology of Microorganisms, USSR Academy of Sciences, Pushchino, Moscow Oblast; State Scientific Research Institute of Standardization and Testing of Medical Biological Preparations imeni L. A. Tarasevich, USSR Ministry of Public Health, Moscow]

[Abstract] The microorganism pseudomonas lytica, when grown on a medium containing yeast extract, casaminic acid and killed staphylococcus cells, synthesized and secreted an enzyme which lysed the staphylococcus cells and the cells of other gram-positive microorganisms. This article studies the bacteriolytic activity of the enzyme preparation isolated from a pseudomonas lytica VKM V-1494 culture for various groups of pathogenic and opportunistic microorganisms. All the gram-positive microorganisms tested were lysed, staphylococci being the most sensitive to the substance. The results indicate the possibility of using the substance to treat a number of diseases caused by pathogenic staphylococci, including infections of wounds, burns and other skin traumas. Figure 1, references 20: 4 Russian, 16 Western.

Breakdown of Phosphoinositides and Formation of Diacylglycerin in Human Thrombocytes Caused by Lipopolysaccharide Toxin

18400496A Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104 No 3, Mar 88 (manuscript received 17 Mar 87) pp 291-294

[Article by A. B. Viktorov, Ye. Kh. Dank, V. A. Kuznetsov, V. G. Ter-Simonyan and V. A. Yurkiv, Central Scientific Research Institute of Epidemiology, USSR Ministry of Public Health, Moscow]

[Abstract] Lipopolysaccharide toxins can activate the blood coagulation system, possibly by acting directly on the thrombocyte link of the system. This article studies the influence of lipopolysaccharide toxin on plasma membrane structure, the phosphoinositide cycle, endogenous phospholipase activity and thromboxane B_2 synthesis in human thrombocytes taken from donor blood, washed, suspended and studied within three to four hours after extraction. The functional status of the thrombocytes was determined by studying aggregation initiated by Merck thrombin. Although the toxin resulted in decomposition of a significant fraction of the phosphoinositides (15-30 percent) and formation of large quantities of diacyglycerine (20 percent), aggregation of thrombocytes did not occur. This indicates that phophoinositide cycle activation is probably not a necessary and sufficient condition for induction of thrombocyte aggregation. Figures 3, references 12: 2 Russian, 10 Western.

UDC 591

Biological Activity Spectrum of Secretory Products of Human B-Cell Lymphoblastoid Line RPMI-6410t

18400504 Moscow ONTOGENEZ in Russian Vol 19 No 3, May-Jun 88 (manuscript received 9 Mar 87) pp 240-246

[Article by T. M. Seregina and M. I. Mekshenkov, Institute of Developmental Biology imeni N. K. Koltsov, USSR Academy of Sciences, Moscow]

[Abstract] It was shown that the lymphoblastoid line of human B-cells RPMI-6410t secrets a factor with a wide spectrum of biological activity. It exhibited growth stimulating activity on human lymphoblasts of the 6410t line and on embryonal diploid fibroblasts. On other targets—lymphoblastoid lines P3HR-I.G5 and Raji (Burkitt's lymphoma)—it had cytostatic and cytotoxic effects respectively. This product is claimed to be similar to human tumor necrosis factor (hTNF) in terms of biological activity and some physicochemical properties. Optimal activity was observed at pH 6-8 and up to 56 degrees C; at pH 2 and 10 the activity decreased by 100 percent and 50 percent, respectively. Heating this factor to 70 degrees C for 1 hour inactivated it completely. Figures 3; references 14: 3 Russian, 11 Western.

Possibility of Quantizing the Kinetic Parameters of Single Ion Channels

18400015a Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 301 No 2, Jul 88 pp 465-469

[Article by V. I. Geletyuk, V. N. Kazachenko, and V. E. Tseyeb, Institute of Biophysics, USSR Academy of Sciences, Pushchino, Moscow Oblast]

[Abstract] Currents were recorded through the fast K^+ channel, with peak-to-peak noise level less than 1 pA. In addition to large-amplitude current pulses, a wide range of lesser-amplitude pulses were observed, which is often due to a varying number of conductivity substates in the pulse. Pulse edges had various forms. Baseline fluctuations did not exceed 10-20 percent of peak-to-peak amplitude. It was established that current pulse width increased with amplitude for a given level of membrane potential. Pulse width τ_0 distributions for amplitude intervals of i, 1-1.5, 4.5-5, and 5.5-6 pA were nonmonotonic, and each had 2-4 absolute maxima. Pulse interval τ_i distributions had the same characteristics as the τ_0 distributions. Δ distributions produced quantifiable values that were multiples of 125 and 250 μsec. Figures 4; references 15: 3 Russian, 12 Western.

UDC 577.352.3:577.344:579.841.51

Coupling of Proton Uptake Process During Bacteriorhodopsin Photocycle With Isomerization of Chromophore Group

18400492 Moscow BIOLOGICHESKIYE MEMBRANY in Russian Vol 5 No 4, Apr 88 (manuscript received 9 Nov 87) pp 400-407

[Article by V. V. Zorina and A. D. Kaulen, Interfaculty Scientific-Research Problem Laboratory of Molecular Biology and Bioorganic Chemistry imeni A. N. Belozerskiy, Moscow State University imeni M. V. Lomonosov]

[Abstract] In earlier studies it was shown that proton transfer by bacteriorhodopsin (BR) occurs in two stages. First, isomerization of retinal (induced by light) leads to deprotonation of retinal aldimine, the liberated proton showing up on the surface of the purple membrane, followed by formation of the M intermediate. At the second stage, retinal aldimine picks up a proton from the opposite side of the membrane. Upon absorption of a quantum of light, the chromophore group isomerizes from the all-trans state to the 13-cis state. Retinal aldimine deprotonates during the conversion of the intermediate L to the intermediate M. The key feature in further relaxation of bacteriorhodopsin into the initial state (bR) is the reprotonation of retinal aldimine before the reverse cis-trans isomerization of the chromophore group and capture of the available proton. This occurs during M-intermediate conversion to P-intermediate. The absorption maximum of the P intermediate is at 560 plus or minus 5 nm, with an extinction coefficient of 70 plus or minus 10 percent of that of the bR α-peak. In comparison to the initial form of bR, the P-intermediate shows greater absorption value at 330-350 nm, possibly corresponding to the β-peak of the 13-cis retinal chromophore group. Figures 7; references 13: 5 Russian, 8 Western.

UDC 632.3

Biotechnological Methods of Creating Virus-Free Plant Stocks in the USSR

18400017 Moscow VESTNIK AKADEMII NAUK SSSR in Russian No 6, Jun 88, pp 19-25

[Article by I. G. Atabekov, Corresponding Member, USSR Academy ofSciences]

[Abstract] One of the most effective measures for protecting plants from viruses is to heal infections and continue cultivation of plants in conditions which prevent reinfection. One of the most effective means is to extract meristematic tissue free of viruses or containing only small concentrations of viruses and to then regenerate entire plants from these cells in the laboratory, which are then reproduced in the required number. These techniques, combined with heat treatment, can yield virus-free plant stocks for agricultural use. Diagnosis of infected plants is an important stage in virus-free seed stock maintenance for potatoes, fruits, grapes and flowers. Objective evaluation of the quality of plant materials is impossible without the use of modern immunodiagnosis methods which, unfortunately, were not developed in the Soviet Union until quite recently. External and internal quarantine measures to protect agriculture from the importation of viruses are also important. A combined system of large-scale agricultural plant virus diagnosis has been developed in the framework of the Biotekhnologiya program by units of the USSR Academy of Sciences, the Academy of Agricultural Sciences imeni Lenin, Agroprom USSR, and Minelektronprom. The system uses highly sensitive, high-speed mass diagnosis methods and methods for producing highly pure antigen preparations for deriving diagnostic antisera. The diagnostics are automated. Pure viral antigens for potatoes and a number of other crops have been developed on the basis of immunoenzyme analysis for the creation of highly specific diagnostic preparations for more than 20 viruses. A bacterial virus agglutination test has now been introduced at a number of farms, and a new, nonimmunologic method of diagnosis has been developed, based on genetic engineering principles that use molecular cloning of the genome of a virus or a viroid and then DNA probes for diagnosis via molecular hybridization. One of the aims of the Biotekhnologiya program was to develop the technology and manufacture of diagnostic kits for supporting virus-free potato seed stocks based on the new methods. Diagnostic kits based on immunoenzyme analysis are now in production for six of the most important potato viruses (X, Y, S, M, L, and F). The Minisry of Electronics Industry, in cooperation with Moscow State University, has developed and manufactured a system of instruments and devices supporting the entire diagnostic process. Figure 1.

Biotechnological Aspects of Applications of Bacterial Bioluminescence In Medicine

18400490c Moscow ANTIBIOTIKI I KHIMIOTERAPIYA in Russian Vol 33 No 4, Apr 88 (manuscript received 9 Jun 86) pp 304-308

[Article by V. S. Danilov and N. S. Yegorov, Moscow University imeni M. V. Lomonosov]

[Abstract] Many chemiluminescent reactions can be used to produce highly sensitive biosensors for use in various fields, including medicine. Bacterial bioluminescence is considered the most promising. This review studies the biotechnological aspects of the application of bacterial bioluminescence to medicine, from the selection of microorganisms, their cultivation, and the isolation of luciferases to the creation of various biosensors. Examples are presented of the determination of biologically active substances and enzymes in biological specimens, featuring high sensitivity of analysis (many orders of magnitude greater than spectrophotometry and even fluorimetry); stable luminescence and high specificity; and rapid, inexpensive analysis on simple equipment. References 52: 2 Russian, 50 Western.

Health and Environmental Pollution In LiSSR

18400462 Vilnius KOMMUNIST in Russian
No 5, May 88 pp 87-92

[Article by LiSSR Chief Health Officer Stanislovas Tarbunas: "Human Health and Ecology Problems"]

[Text] Perfecting the Soviet health care system does not mean merely improving treatment, but most important, it means preventing illness. Therefore, preventive efforts are given primary emphasis in the Basic Guidelines for the Development and Restructuring of the Country's Public Health Care in the 12th Five-Year Plan and the Period up to the Year 2000.

The spread and even the course of any particular disease depends on specific risk factors. We can assert on the basis of scientific research that eight to ten percent of the status of public health is attributable to deficiencies in the public health system, inferior medical service, and ineffective preventive measures. Forty-nine to 53 percent is due to harmful habits, poor nutrition, severe working conditions, the effects of urbanization, and social and psychological factors. Eighteen to 22 percent is attributable to genetic and biological factors (inherited diseases and congenital disability), and 17 to 22 percent is due to environmental pollution, harmful substances, radiation such as cosmic or magnetic radiation, and meteorological factors.

Thus, prophylaxis is not limited to narrow, inter-departmental health care tasks, although even now ministries and departments of the republic as well as local soviets of people's deputies underestimate the significance of prevention and frequently are content with the issuance of decrees and documents of intent instead of adopting active measures to safeguard public health. There frequently has also been a lack of resolve on the part of medical personnel, particularly in hospital services.

The present situation compels us to keep in mind the thought expressed by Academician of the USSR Academy of Medical Sciences V. Kaznacheyev to the effect that medicine without ecology is ineffective. Persons in the medical profession in various countries with highly developed health care have concluded that the continued construction of hospitals with greater bed capacities and a comprehensive program of mass health screening of the population are no longer able to accomplish the desired goal of lowered morbidity. Only a completely vibrant environment is capable of guaranteeing that people are healthy and productive. Recent positive demographic trends in our republic warrant attention. These include the increase in the population, a higher birth rate, a higher natural growth rate of the population, and a significant reduction in the infant mortality rate (ours was the lowest in the country in 1986). However, the death rate did increase (with the exception of 1986, when strict measures were taken to overcome alcoholism and drunkenness and when this index was 9.2 percent lower than it was in 1985), and the average life expectancy did not increase. It was 71 years (65 years for men and 76 years for women). During the last 15 years the number of cardiovascular patients in the republic increased by 4.5 times. Cancer patients increased by a third, including diseases such as skin cancer, which increased by 47 percent, and cancer of the lungs, bronchi, and trachea, in which category there was a 69 percent increase. There has also been an increase in mortality due to congenital diseases.

In spite of some positive moves in environmental protection, the ecological situation of the republic remains unsatisfactory in a number of cities and industrial centers. It is particularly unfavorable in the central and northern regions of Lithuania, where there is a concentration of chemical and petroleum-refining industry plants as well as construction material plants. According to data of the LiSSR State Statistics Committee, 2.3 million tons of pollutants were released into the atmosphere during the last five-year plan, and since that period that quantity has been reduced by just 47 thousand tons. The smokestacks of the Lithuanian GRES imeni Lenin alone release about 110 tons of pollutants yearly, in addition to the "contribution" made by the Akmyantsementas industrial association, motor vehicles, untreated sewage, and chemical contamination of the soil, water, and food products.

Air pollution constitutes one of the principal ecological problems. People can protect themselves against contaminated water, soil, and food products, but not against polluted air. Moreover, various contaminants in the air and in the workplace not only produce effects individually at the time, but, by entering into chemical compounds, manifest their injurious effects five to seven years later.

An analysis of data and facts collected by epidemiology, microbiology and hygiene, and oncology institutes as well as medical epidemiological stations has shown that the deterioration in the health of residents in Kedaynyay, Ionavy, and Akmyane coincided with the onset of the intensive development of the chemical and other industries. Thus, the concentration of pollutants in the effective area of the Keday Chemical Plant 15 years ago was approximately 10 times greater than the permissible level. Although there has been a recent significant improvement in that situation, that level of pollution adversely affected the health of those who lived near the plant at that time.

There are several hundred carcinogenic agents known at present, including benzpyrene and nitrosoamines. The Ionavy Azot industrial association releases such a large quantity of chemical pollutants into the air, that the concentration of ammonia, formaldehyde, sulfur anhydride, nitrogen oxides, and hydrogen fluoride far exceeds the permissible norm even beyond its effective sanitation zone. The air, sediment, soil, and vegetation have been shown to contain benzpyrene, whose concentration

has been gradually decreasing but reaches the natural background levels only at distances of from eight to 12 kilometers from the plant. Even at a distance of eight kilometers from the plant the concentration of volatile nitrosoamines exceeds the normal background level by 10 to 50 times. Research has shown that persons who live near a plant (within five to six kilometers) are one and one-half to two times more liable to suffer diseases of the upper respiratory tract and lungs as well as corneal inflammation and allergic diseases. Children within a five-kilometer zone of the Akmyane Cement Plant were shown to suffer from upper respiratory catarrh, skin inflammation and corneal inflammation three to five times more frequently than children in a control group.

A study sponsored by the USSR Ministry of Health of the effect that air pollution has on the health of Vilnius residents showed that total morbidity of the population in the industrial southwestern region, where air pollution, for example, was nearly double that of the Antakalnis region, was approximately 1.3 times higher. The morbidity rate for acute respiratory diseases was 1.4 times higher, and the skin disease rate was 1.5 times greater. Studies of this nature are now being conducted by the epidemiological stations at Kaunas, Klaypeda, and Shyaulyay.

The situation in the impact zone of the Mazheykyay Petroleum-Refining Plant is a cause of great concern. The concentration of injurious substances such as formaldehyde, sulfur and nitrogen compounds, toluene, and benzene (within one to four kilometers from the plant) exceeds the permissible limits by two to ten times. The Varduva and Venta rivers as well as Lake Seda have been significantly polluted by petroleum products. In the opinion of scientists, the plant is adversely affecting the environment even at a distance of 24 kilometers from the plant. All of this will have a deleterious effect on people's health in a few years or after as much as 10 years unless emergency measures are taken quickly to protect the environment.

Therefore, health indices cannot be improved simply by strengthening the base of medical institutions or increasing the number of physicians and middle level medical personnel (visits to polyclinics now number 44 million annually); nor are they improved merely as a result of the rather high level of mass medical screening of the population and available medications for which each one of us pays a little more than 20 rubles per year.

Some localities in the republic have been adversely affected by the lack of long-term planning (yet to be approved even now) for the construction and expansion of industrial enterprises and installations which have a negative impact on the environment. We have selected construction sites, measured distances, and moved residents out of health-restricted zones in accordance with projected production volumes and technology. In the meantime, enterprises have expanded and new plant production has started even before construction of the plants was completed. This is what happened to the Azot industrial association, and the same thing is happening at the Mazheykyay Petroleum-Refining Plant (we do not yet know what else will be built on the designated area) and at other places as well. And where is the gas fuel that was planned for the Lithuanian GRES imeni Lenin, the Vilnius TETs-3, and other facilities that pollute the environment? Much of the blame for this situation rests with the planning organs, the ispolkoms of the soviets of people's deputies as well as with the design engineers at various national and republic design institutes who thus far bear virtually no responsibility for the quality of their designs or for the solutions (which have not always been dependable) that they propose. One would think that greater influence here might be exerted by the republic's Gosstroy and those of its subdivisions that are responsible for appraising these projects. The quality of the latter can be rather well characterized by the following act: In 1986 health officers did not approve 142 projects (18 percent of those examined), because the projects did not include effective measures for safeguarding the environment against pollution sources or for ensuring proper working conditions. Almost one-half of the projects were rejected last year by the Sanitation-Epidemiology Administration of the republic's Ministry of Health.

The Sanitation Service in concert with the State Inspectorate for Air Protection in the LiSSR assessed stricter penalties against persons violating the law as well as the established sanitation norms and rules. During the last year alone, environmental pollution and harmful working conditions served as the basis for closing four granulating mills of the nitrophosphate shop of the Ionavy Azot association and the foundries of the Kaytra Medical Supplies Plant. In addition, production was halted at the Kaunas Railroad Tie Impregnation Plant and at the Kedaynyay Electrical Equipment Plant. Permission was denied for the construction of a glass-founding furnace without air cleaners at the Panevezhis Ekranas Plant. This compelled the supervisors at those plants as well as the supervisor of the Klaypeda Paper Pulp and Carton Plant to take immediate measures.

The position of the sanitation service is the following: Until such time as the enterprises build and install decontamination facilities that meet all the necessary requirements, there must be no further expansion at the Kedaynyay Chemical Plant, the Azot and Akmyantsementas associations, the Mazheykyay Petroleum Refinery, and other enterprises which would otherwise be totally unable to prevent the release of harmful chemical substances into the air, the soil, and the water at levels that exceed the permitted norm.

Data of the World Health Organization indicate that if the level of air pollution were reduced by one-half, the average longevity of residents would increase by three to five years, the average morbidity and mortality figures would be reduced by four to five percent, the number of patients with lung cancer and other respiratory diseases would decline by 20 to 30 percent, and there would be a

10 percent reduction in the number of patients with cardiovascular diseases. Therefore, the republic program "Health to the Year 2000" calls for a reduction in the pollution of the air, soil, water, and food products, the adoption of rational nutrition principles and a healthy life style, which would thus result in a two- to three-year increase in average longevity... It goes without saying that this program cannot be fulfilled without constant effort on the part of the party and planning organs, the ispolkoms, ministries, and departments.

Another important problem that requires resolution is the sanitation of drinking water and recreational sites. Our republic is the only one in the country that uses ground water for drinking purposes. It can be said that the quality of that water (i.e., its bacteriological content) does not now constitute a threat to public health. Therefore, there has been a significant reduction in the number of infectious diseases that were previously spread via this medium. However, we still do not know how to protect the water against viral contamination. This is apparently one of the reasons for the spread of hepatitis A in Alitus, Shyaylyay, Panevezhis, Vilnius, and in the Kedaynskiy, Shirvintskiy, and Vilkavishksiy rayons.

There has been a decrease in the chemical contamination of water. This improvement has occurred because the sanitation service has not permitted the construction of new water diversion structures or expansion of old ones without the installation of iron-removing equipment. Nevertheless, there are still 57 operating water diversion structures in the republic whose iron content exceeds the established limits. The construction plan for such installations as approved by the LiSSR Council of Ministers must be followed to the letter.

Of serious concern is the fact that over 1.5 million inhabitants of the republic (in cities such as Vilnius, Kaunas, Panevezhis, Druskininkay, Alitus, Trakay, Lentravis) are using water that does not contain a sufficient amount of fluoride, whereas approximately 300,000 people in Klaypeda, Kretinga, Salantay, Kelme, Palanga, and other cities and settlements are using water that is supersaturated with fluoride. It is essential that we immediately design and implement technology for the fluoridation of water as well as the defluoridation of water, since we have had a significant increase in the incidence of caries and other dental diseases associated with either a deficiency or an excess of fluoride in the water.

Studies at the Geology Institute have shown that the amount of nitrates in the water table is directly proportional to the use of nitrogen fertilizers. And as we know, those waters feed into the shaft wells and drinking water used by one-third of the republic's population. Last year, the sanitation service's inspection of almost 3,200 public and private wells showed that 15 percent of the tested wells had elevated nitrate concentrations (21 percent had such concentrations in 1986). In such cases, we require that fresh water be brought from other places, that wells be pure, and that well contamination be brought to a halt. This must be kept in mind by supervisors of city, rayon, and district soviets of people's deputies, farms, and organizations as well as agro-industrial associations. More caution should be exercised by residents themselves who bring nitrogen and organic fertilizers to their private plots located near wells.

Tests of river and lake water at vacation sites have shown that the level of their chemical contamination has decreased during the years 1981-1987 from 20.3 percent to 13.8 percent, and that bacterial contamination has decreased from 30 to 27 percent. However, the cleanliness of the water along the sea is deteriorating, particularly at the resorts of Palanga, Shventoyn, Smiltine, Melnraga, and Girylyay. Swimming should be prohibited in certain places, particularly at Melnraga. The beaches on the Nyamunasa in Druskininkay, Kaunas, and other cities have also become substandard. At the present time, only 62 percent of the more than one million cubic meters of contaminated sewage is treated at decontamination facilities, and less than one-fourth of the sewage is decontaminated in accordance with the established standards.

Our republic has approached the levels of the developed European countries with respect to the amount of fertilizer being used per unit of land, but still considerably lags behind those countries with respect to the efficient utilization of fertilizer. The Lithuanian Scientific-Research Institute for Agriculture has devised an efficient procedure for the application of fertilizers to agricultural crops. However, that procedure is frequently not observed. Mineral fertilizers are stored improperly, inasmuch as only one-fifth of the warehouse facilities has been constructed in accordance with the standard plans. Therefore, a large quantity of fertilizer is washed by rain into the soil and the water table and is carried into open reservoirs. When fertilizers are improperly utilized, plants do not assimilate the nitrogen, and it accumulates in vegetables, fruits, and greens as well as in meat, milk, and other products in the form of nitrates.

When nitrates enter the body through food and water, they are converted to nitrites, which then combine with amines to form nitrosoamines, many of which are carcinogens. An excessively high nitrate content leads to the intoxication of hemopoietic and endocrine organs as well as to cerebral and immune system disturbances. Nitrates can also cause acute intoxication (particularly in breast-fed infants).

Prior to 1986 there was almost no reduction in the nitrates contained in vegetables. For the most part, nitrates were contained in cucumbers, potatoes, and cabbage. The Ministry of Health sounded an alarm about this matter, and the republic's Council of Ministers obligated the State Agro-Industrial Committee to take decisive measures. An inter-departmental commission was formed to coordinate efforts in this area. In addition, the State Agro-Industrial Committee placed greater

demands upon farm supervisors, which yielded rather good results. Last year, the sanitation epidemiological stations found that only 13.3 percent of 3,381 tested vegetables did not meet the established standards. Thus, in the public sector we were able to cultivate a normal crop for 98 percent of our cucumbers, 97.5 percent of the potatoes, 94 percent of the cabbage, 99.6 percent of the beets, 96.5 percent of the onions, and 97.7 percent of the scallions. Those products are being sold without any restrictions or special warnings. The hothouse vegetable situation has also improved. Thus, after successful efforts, the farms of the republic and the agro-industrial complex can now supply us with good vegetables and products, without any need to make concessions in connection with the notorious "unfavorable weather conditions."

After having examined approximately 440 daily food rations, we can assert that nitrate content in foods did not exceed the established norm as a whole. Environmental contamination by chemicals will also be reduced, since toxic chemicals will no longer be applied by aircraft.

There is an increasing number of ecological problems associated with agricultural sites such as settlements, cattle breeding complexes, petroleum product and pesticide warehouses, and, frequently, poorly designed engine yards and dumping grounds. Poor management has also had adverse effects. Therefore, dangerous levels of pesticides have frequently been found in food products, and inhibitor substances have been found in milk, and sometimes harmful working conditions have caused occupational illnesses.

One must not think that environmental protection and ecological problems are merely the concern of the appropriate official organizations and departments. Ecological quality is essential to every person. It is painful to see garbage along the edges of forests and old tires scattered along roads. At times you see an owner who would have to wash his car on a picturesque shore of a lake. We have become accustomed to thinking that someone is supposed to take away the discarded garbage, and we have come to believe that we have done our duty by reporting this to the inspection authorities. Or, for example, supervisors of departments, organizations, enterprises, and farms are annoyed by the interference of inspectors, although they don't seem to be concerned about proper procedures without some urging. Perhaps that is why we have so many inspectors—in order to have someone upon whom to dump the responsibility for unresolved problems.

The party, soviet organs, and all persons involved with environmental protection services and organization have found a solid support for enabling them to set trends in the right direction. I have in mind the recently adopted decree of the CPSU Central Committee and the USSR Council of Ministers on a radical restructuring of nature conservation in the country. That lever must be utilized to the fullest extent. We hope that the sanitation service too will finally be allowed to fulfill its direct obligations, and not merely be occupied with garbage cans, stopped up basements, toilets...

Humanity is confronted by the threat of nuclear war and the threat of an ecological catastrophe. A great deal of effort has recently been made to preserve the peace. But we should not forget for a single minute that no less a dangerous fate awaits us if we are not able to preserve an environment that is favorable to humankind and we are not able to preserve the harmony of nature.

UDC 612.014.482:614.7

Hygienic and Medical-Biological Aspects of Strontium-90 Contamination of the Environment

18400019 Minsk ZDRAVOOKHRANENIYE BELORUSSII in Russian No 3, Mar 88 (manuscript received 2 Jul 87) pp 62-64

[Article by V. I. Ternov, Belorussian Institute for Advanced Training of Physicians]

[Abstract] The problem of environmental contamination with the radioactive isotope strontium-90 arose in the 1950s in connection with nuclear weapons testing in the atmosphere. Sources of strontium today include nuclear weapons testing, operation of nuclear reactors used for various purposes, and possible accidental releases of radioactive products at hazardous radiation sites, including nuclear power plants. Strontium-90 presents its greatest danger to the human body when it enters the food chain and is then ingested in the body. The biological effects and mechanisms by which food products may become contaminated with strontium-90 are discussed. Until recently, the degree of environmental pollution with radioactive strontium was such that no special protective measures were required. However, experience has shown that in some situations it may be necessary to limit the entry of radioactive products into the human body, in which case both radiation doses and the number of persons exposed to radiation must be limited as much as possible. "Critical" food products—the primary food products through which strontium-90 enters the food chain—must be determined if the migration of radionuclides into the human body is to beinterrupted, and protective measures must be introduced at various stages of food production,processing, and distribution. References 19 (Russian).

New Method for Plant Growing

18400463a Moscow ZNANIYE-SILA in Russian No 6, Jun 88 pp 38-39

[Article by Yu. Gaydukov: "Is It Worth It for Herbs to Jog?"]

[Text] Just imagine, dear reader, the following picture. You are sitting in a movie theater and you see an egg on the screen. It contracts, expands, and starts to vibrate. The opening egg shell crackles, and the top of the egg flies downward. But instead of a chick coming out of the shell, there is a green sprout! After tottering for awhile, it comes out and makes its first unsteady steps. Phantasmagoria? Only in part. And now a little prologue to the story about what was accomplished by candidate of technical sciences Valentin Nikolayevich Golovin and his associates at the USSR Academy of Sciences Institute of Biomedical Problems (IMBP). In essence, the investigators asked themselves, is it really necessary for plants to move? To which they replied in the affirmative.

Why should plants move? The whole crux of the question lies in the fact that conventional plantings carefully nurtured by a gardener waste sunlight and heat.

Take, for example, sprouts in beds. One shoot is separated from the other by areas of bare earth, and it is only in vain that the sun dries out the black soil. Or take the other extreme: When neighboring plants are inefficiently seeded, they vigorously compete for light and space. Who hasn't planted carrots, let us say, at a dacha? We spread the seeds imprudently and generously, and the sprouts develop into a thick growth of carrot stems. Later it becomes necessary to thin out the plantings and remove a part of the plants. "The more the merrier" is not an applicable proverb for plants.

Soil and light can be fully utilized by placing the plants in sliding mechanical accordion-rows. At first the crops are seeded in tightly compressed rows, and later, depending on how broad the plants' leaves become, the "accordion" is extended. As they are moved around, the plants get as much space as they need at a given period of their development.

At first, the line of thinking of the scientists at the IMBP did not seem to be especially original, but the preeminence of the next step was indisputable. The researchers planted vegetation of all ages in a row according to the degree of their development. The plants were then positioned on a long tape in order of age and, consequently, by the extent of growth. Now the bellows of the "accordion" must be extended unevenly. There were only a few plants in the first rows, where the young sprouts were growing, whereas the last rows, which contained the mature growths, had many more plants.

The seeds in the apparatus were not sown in soil or even into soil substitutes, but rather on a conventional polyethylene film which was inserted into cassette holders. Looking at the rows of cassettes from the side, one can see a green ridge, which indicates a transition from the weak shoots at the beginning of the track to the adult plants at the track's end.

The length of the tape depends on the time required for the plants' maturation. Let us say this takes one month. This means that the shoots must make 30 steps to get to the harvest period (the cassettes are shifted manually or with the aid of a motor).

A shoot "steps ahead" 30 times. The lamps are turned on and off the same number of times. Thus, morning gives way to evening, and vice versa. Exactly one month later, the laboratory technicians can harvest the mature plants at one end of the tape.

The Moscow scientists utilized the very latest hydroponics technology to build the conveyer-field. A nutrient solution whose level was slowly raised, with the roots gradually submerged, was fed into the cassettes every hour, thereby supplying the roots with water and mineral salts. The solution contained optimal concentrations of all the elements essential to growth (16 elements in all). Then, after the "expiration" phase, the "inspiration" phase began. The moisture level in the cassettes was gradually lowered. The residues of mineral substances are then used in the next cycle. And the dehumidified roots can still breathe atmospheric oxygen.

The first advantage of this apparatus is that the harvesting process is continuous. There are no seasons to be concerned about. Moreover, the conveyer offers a radical solution for the problem of storage. One can produce exactly as much green as is required every day (or hour or minute, depending upon the length of the column). This most important property of the track was, understandably, of inevitable interest to those were were getting ready to send cosmonauts on prolonged space flights.

So far, the devices (they were first made for space operations) have not yet been approved for manufacture, although there are uses for them already. After all, there are quite a few places on earth where the circumstances are almost the same as those in space. For example, a compressor station on a gas line in some Siberian marsh out in the middle of nowhere. Or a meteorological station located high atop some mountain.

Space greenhouses rapidly gained acceptance first and foremost in the North. Specialists from the IMBP built compact devices at the request of polar research workers. These mini units the size of a writing desk with a field area of half a square meter were called "Arctic Self-Growers." The devices require only three minutes a day for servicing. The operation of the devices is simple. The harvested crop is removed, a new cassette with seeds loaded, and a daily dose of mineral salts injected, all with the simple turn of three handles.

Today there are dozens of such devices being used for the cultivation of greens in the Arctic.

In agriculture as in sports, harvests do grow, but slowly. There have been some gratifying achievements, but no stability. Not so with the phytoconveyer. Hydroponics technology here is saving considerable water and fertilizers, and the movement reduces the expenditure of radiant energy and sowing area.

And what about the harvest level? The devices have consistently demonstrated high-level results—over 500 grams of greens per day. The size of the fields is half of a square meter. This means that one can get more than a kilogram from each square meter (in the winter, for example, one can also grow one kilogram of parsley from a square meter in hothouses, but in a month's time).

Comprehensive studies have been conducted over many years at the IMBP. Greenhouses have been provided with phytoconveyers from one and one-half to 20 meters in length. If calculated per hectare, up to three and one-half tons of greens have been harvested in a day. The fields yield 50 tons, but that is for the whole season! These devices can also be made into multi-tiered conveyers, which would significantly increase the total sowing area. The conveyers could also be installed in plant shops [zavodskiye tsekhi], in corridors of industrial enterprises and organizations, and even in basements. One square meter of a conveyer under artificial light can yield enough greens per day for ten to twenty persons.

Hothouse versions of the devices have been built and tested in long-term experiments. One can see by inspecting and handling these devices that their design is not complex, that they are not expensive, and that they are easy to operate. Scientists and design engineers believe that their operation is already outmoded. The scientists have gone on to making conveyers which operate not under artificial light, but natural light. Experiments have been conducted in the Crimea near Simferopol. Six 30-meter conveyers for growing alfalfa and soybean have been operating under open skies for several years. From 700 to 1,400 tons of greens per hectare have been harvested during the growing season.

The new method of cultivating plants requires less labor expenditure and less energy expenditure of agricultural machinery than is required when vegetation is cultivated in the soil. The new method results in a saving of water and fertilizer and practically does away with the need for weed control as well as herbicides. And all this is attributable to what was done by V. N. Golovin and his associates. Of course, these are only the first "attempts at writing." It is still too early to come up with conclusive results. But scientists already have their sights on the distant future. In particular, there is a plan for cultivating forage crops on an industrial basis. This will require a network of phytoconveyers having a total area of hundreds of square kilometers

UDC 579.842.15:579.252.5].575.113

Gene Library of Shigella Sonnei Plasmid pSS120

18400081a Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 7, Jul 88 (manuscript received 17 Jun 87) pp 20-23

[Article by T. S. Belova and Yu. M. Romanova, Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamalyeva, USSR Academy of Medical Sciences, Moscow]

[Abstract] A gene library was constructed for plasmid pSS120 of Shigella sonnei IHP-941, since this plasmid bears invasiveness genes and genes determining the phase I species-specific antigen, the expression of which is required for full virulence of Sh. sonnei. The library was based on the use of plasmid pSL5 as a vector. pSL5 is a hybrid of phage lambda 47.1 and plasmid pUC19, and retains the phage genes needed for lysogeny or lytic development depending on the culture conditions. The restriction enzyme EcoRI was used for complete restriction analysis of pLS5 DNA and for partial analysis of pSS120 DNA. Following ligations, the DNA preparations were packed in vitro into phage lambda capsids. The phage titer on E. coli LE 392 was 0.8×10^3 clones/μ DNA of plasmid pSS120. A total of 250 clones was identified. Based on an average insert of 8.9 tp, the detection of a given gene with 99 percent probability would require analysis of 92 recombinant clones. Figures 2; tables 1; references 9: 4 Russian, 5 Western.

UDC 615.372:579.843.1].015.4:612.017.1].076.9

Interserovar Antitoxic Immunity Against Cholera Toxins

18400081c Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 7, Jul 88 (manuscript received 29 Apr 87) pp 43-46

[Article by L. G. Belov, A. K. Adamov, V. P. Avrorov, V. L. Kulikova and Ye. V. Glyanko, All-Union Scientific Research Antiplague Institute "Mikrob," Saratov; Scientific Research Antiplague Institute, Rostov-on-Don]

[Abstract] Cross-immunity studies were conducted with cholera toxins derived from the Inaba and Ogawa serovars of the cholera vibrio, in view of the fact that immunization with Inaba vaccines protects against both Inaba and Ogawa, whereas Ogawa vaccines offer little protection against Inaba. The studies on rabbits and mice were conducted with toxins derived from Inaba 569B and Ogawa 1310 producing fairly high levels of the toxin. Studies on rabbit intestinal loop and rabbit and mouse skin tests demonstrated that the Ogawa toxin was 2.5-fold less choleropenic and 16-fold less potent in terms of cutaneous permeability that the Inaba toxin. Only the Inaba toxin induced local immunity in the rabbit intestine against both toxins, while the Ogawa toxin failed to protect against itself and the heterologous toxin. The Ogawa toxin was less immunogenic than the Inaba toxin, with the Ogawa antitoxin was less immunogenic than the Inaba toxin, with the Ogawa antitoxin neutralizing only the Ogawa toxin. The Inaba antitoxin neutralized both toxins. These findings point to both antigenic similarities and obvious differences in the two toxins that are also reflected in the inducted antibodies. The exact nature of these differences may involve allosteric antigenic changes, although definitive studies must await purified preparations of the toxins. Tables 3; references 15: 8 Russian, 7 Western.

Relationship of Biological Activity of Double-Stranded Interferon Inductors to Their Penetration into Cells and Protein Synthesis Suppression

18400490b Moscow ANTIBIOTIKI I KHIMIOTERAPIYA in Russian Vol 33 No 4, Apr 88 (manuscript received 17 Jun 86) pp 275-280

[Article by N. A. Radomskaya, T. M. Sokolova, F. I. Yershov]

[Abstract] Results are presented from a study of the conditions of penetration of double-stranded inductors into cells and their interaction with cell structures. The variation of biological activity with degree of cell penetration and its influence on the synthesis of cell proteins are studied for the first time. The studies of the penetration of ^{125}I-labeled double-stranded inductors compared three types of processing: addition of inductors to phosphate buffer, addition to DEAE-dextran solution, and as a precipitate in calcium phosphate. Cell binding of the inductors was highest by far with the third method. Protein synthesis was inhibited in mouse cells but not in human cells. Antiviral activity increased by 1 to 3 orders of magnitude; interferon production, by 2 to 4 times. References 9: 5 Russian, 4 Western.

Immunomodulating Effect of Substances Activating and Blocking the GABA-Receptor—Ionophore Complex

18400495d Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 51 No 3, May-Jun 88 (manuscript received 27 Feb 87) pp 78-80

[Article by L. V. Devoyno and I. O. Beletskaya, Institute of Physiology, Siberian Division, USSR Academy of Medical Sciences, Novosibirsk]

[Abstract] Experiments were performed on 280 CBA mice immunized with sheep erythrocytes. The immune response was determined by the number of rosette cells per 1000 nucleus-containing cells in the spleens of the mice. The direct GABA-receptor agonist mucimol, the competitive GABA-receptor inhibitor bicuculline and the Cl-ionophore blocker picrotoxin were administered individually and in combinations. Mucimol at 0.5 and 1 mg/kg increased the number of rosette-forming cells in the spleen on the fifth day after immunization. Bicuculline at 0.5 mg/kg suppressed the immune reaction, halving the number of rosette-forming cells. A combination of the two caused no immune reaction stimulus. Picrotoxin also had an immunosuppressive effect at 0.5 mg/kg. Figure 1, references 11: 6 Russian, 5 Western.

UDC 615.849:002.6]:681.31

Development of an Automated Data Retrieval System for Radiology

18400501b Moscow MEDITSINSKAYA RADIOLOGIYA in Russian Vol 33 No 5, May 88 (manuscript received 23 Feb 87) pp 61-64

[Article by I. G. Zhakov, V. Ye. Kratenok, K. P. Gorelko, and N. V. Leoshkevich, Scientific Research Institute of Oncology and Medical Radiology, BSSR Ministry of Health, Minsk]

[Abstract] An automated data retrieval system (ADRS) was developed for the area of oncologic radiology. The data base was created from the existing All Union Scientific and Technical Information Institute "Biologiya" data base—which includes more than 1,000 periodicals, as well as books, patents, and symposia and conference papers in 26 languages, from 46 countries—and its "Radiatsionnaya Biologiya" and "Onkologiya" data bases. Existing ASOD software packages were used with the YeS-1022 computer. The system provides 1) selective dissemination of information based on 194 fixed user requests, 2) personal search in the dialogue mode, and 3) data file update. Plans include enlarged coverage of new topic and introduction of new programs. References: 2 (Russian).

UDC 615.385.1.014.413.036.8

First Experience in Clinical Use of Erythrocyte Mass Resuspended and Preserved in Eritronaf Solution

18400502a Moscow GEMATOLOGIYA I TRANSFUZIOLOGIYA in Russian Vol 33 No 6, Jun 88 (manuscript received 7 Dec 87) pp 7-12

[Article by V. A. Agranenko, I. A. Suvorova, V. Yu. Zorenko, V. L. Golubeva, F. R. Chernyakhovskiy, Yu. G. Miterev, L. A. Zherebtsov, and R. N. Shishina, All Union Hematological Scientific Center of USSR Ministry of Health, Moscow]

[Abstract] A new solution (Eritronaf) was developed at the All Union Hematological Scientific Center of the USSR Ministry of Health for the preservation and resuspension of erythrocyte concentrate and erythrocyte mass (EM). Clinical evaluation of EM resuspended in Eritronaf was carried out at the All Union Hematological Scientific Center; at the Byelorussian Scientific Research Institute of Hematology and Blood Transfusions (A. A. Rakityanskaya, L. S. Torgovtseva, A. A. Novik) and at its counterparts in Kiev (L. F. Romanova, Z. S. Stakovetskaya, I. V. Osadtsiv) and Kirov (D. S. Simkin, N. A. Fedorovskaya, T. N. Beznosikova); and at the Military Medical Academy imeni S. M. Kirov (A. Ya. Plakhotnikov, T. M. Petrenko) and the Latvian Scientific Research Institute of Trauma and Orthopedics (Yu. V. Zhukova). The red blood cell mass was stored for up to 35 days, and posttransfusion reactions were studied in 337 patients with acute and chronic anemia who received transfusions with the EM. It was shown that the EM preserved in Eritronaf was well tolerated and provided an effective transfusion solution. The red blood cells retained their morphofunctional, rheologic, and therapeutic properties. References: 2 (Russian).

UDC 615.385.1.014.07

Biochemical Modification of Erythrocyte Mass Which Lost Its Efficacy After Prolonged Storage

18400502b Moscow GEMATOLOGIYA I TRANSFUZIOLOGIYA in Russian Vol 33 No 6, Jun 88 (manuscript received 1 Jun 87) pp 12-14

[Article by N. N. Tibilova, N. A. Markova, O. N. Yermolchuk, O. V. Platonova, and V. A. Agranenko, All Union Hematological Scientific Center, USSR Ministry of Health, Moscow]

[Abstract] The goal of this study was to evaluate the efficacy of a method developed at the All Union Hematological Scientific Center for "rejuvenating" erythrocytes stored in Eritronaf solution for over 35 days. It was shown that resuspension of red blood cells in Eritronaf solution on the day of its preparation and rejuvenation of the erythrocytes in an Eritropifaden solution made it possible to store RBCs for up to 53 days. The study indicated that it was possible to safely store such rejuvenated blood for 4 days in refrigerators at 4 plus or minus 2 degrees C. The principal values of such stored transfusable blood did not differ markedly from those obtained on the day of blood donation. References 7: 6 Russian, 1 Western.

UDC 615.385.1.014.41.07

Morphological and Functional Properties of Erythrocyte Suspension in Preservative Based on Modified Deionized Gelatin Solution

18400502c Moscow GEMATOLOGIYA I TRANSFUZIOLOGIYA in Russian Vol 33 No 6, Jun 88 (manuscript received 20 Jul 88) pp 14-18

[Article by V. N. Melnikova, V. T. Pleshakov, Ye. A. Selivanov, K. P. Ivanov, T. N. Kartashevskaya, Z. P. Belyayeva, I. M. Krivtsova, I. N. Degtereva, I. V. Botalov, and A. Ye. Chuykin, Scientific Research Institute of Hematology and Blood Transfusion, Institute of Physiology imeni I. P. Pavlov, USSR Academy of Sciences, Leningrad]

[Abstract] A new preservative agent for erythrocytes was developed at the Leningrad Institute of Hematology and Blood Transfusion on the basis of a gelatin deionized on an ion-exchange resin. This agent is an 8 percent solution of a modified, deionized gelatin (MDG) with a molecular weight of 13,000-19,000 D and containing 0.1 percent disubstituted sodium citrate. The morphological and functional properties of erythrocytes stored in the agent were compared with those of red blood cells

suspended in an autologous plasma. In both cases the red blood cells by and large retained their properties after storage at plus 4 degrees C for up to 21 days. The rheological properties of cells kept in the preservative suspension were slightly better than those of cells in the control. Erythrocytes suspended in MDG can be used in place of whole blood in massive blood loss. Figures 2; references: 3 (Russian).

UDC 615.381.014.4.07

Changes in Rheological Properties of Citrate Blood and in Structure of Erythrocyte Membranes During Storage
18400502d Moscow GEMATOLOGIYA I TRANSFUZIOLOGIYA in Russian Vol 33 No 6, Jun 88 (manuscript received 24 Sep 87) pp 18-21

[Article by Ye. D. Buglov, Ye. I. Slobozhanina, G. M. Kostin, I. Ye. Fedorovich, S. L. Bekreneva, S. I. Dovgalev, and Ye. A. Chernitskiy, Belorussian Scientific Research Institute of Blood Transfusion, BSSR Ministry of Health, Institute of Photobiology, BSSR Academy of Sciences, Minsk]

[Abstract] In an earlier work it was shown that the rheological properties of stored blood change. The present work attempts to find the possible causes for these changes. Freshly donated blood was stored in the Glugitsir preservative at 4 plus or minus 2 degrees C for 30 days. Changes in erythrocyte aggregation and apparent blood viscosity began to appear after 1 week of storage and progressed with time. The study indicates that the observed changes in rheologic properties and in the form and deformability of erythrocytes are related to the changes in the protein-lipid interactions in erythrocyte membranes that occurred during storage. Figures 5; references 11: 4 Russian, 7 Western.

Magnetotherapy In Combined Treatment of Patients With Purulent Wounds and Osteomyelitis
18400508a Leningrad VESTNIK KHIRURGIYA IMENI I.I. GREKOVA in Russian No 4, Apr 88 (manuscript received 29 Apr 87) pp 141-143

[Article by V. A. Alyshev, A. L. Vyaznikov, I. G. Gertsen, N. L. Krylov, V. V. Rutskiy, V. L. Royzin, V. V. Serdyuk, A. A. Ushakov and M. V. Shelyakhovskiy, Department of Traumatology, Orthopedics and Naval Surgery, Odessa Medical Institute imeni N.I. Pirogov]

[Abstract] Use of a variable magnetic field with an induction of 20 mT for treatment of trophic ulcers of the lower extremities and infected wounds has been reported. The clinical effect of magnetic fields in treatment of osteomyelitis and purulent wounds results from the direct influence of the field on the pathogen, the influence of the magnetic field on the traumatized extremity tissue by stimulation of separation of necrotic tissue, improvement of vascularization, optimization of processes of regeneration of soft and bone tissues, improvement in tissue oxygenation, stimulation of the immune system and alteration of the properties of medications, increasing their effectiveness. The method of treatment of osteomyelitis under authorship certificate No. 1162443 involves application of a medicinal mixture that includes a five percent novocaine solution containing polyglucin and antibiotics which accumulate in bone tissue, followed by administration of a 10 percent caffeine-sodium benzoate solution and local magnetic therapy with a 25-30 mT, 50 Hz magnetic field, for 25-30 minutes. The magnetic therapy involves 10-15 procedures in all. The method achieved complete elimination of the inflammatory process in bone and muscle tissues, with relief of local pain and complete restoration of freedom of movement, with full recovery in 35-40 procedures. Figure 1, references 12: Russian.

Hemosorption With Xenospleen as Part of Detoxication Therapy of Complicated Trauma
18400508b Moscow ORTOPEDIYA, TRAVMATOLOGIYA I PROTEZIROVANIYE in Russian No 5, May 88 (manuscript received 12 Nov 86) pp 6-10

[Article by M. V. Grinev, Yu. N. Tsibin, G. M. Frolov, M. N. Tarelkina and L. P. Pivovarova, Leningrad Institute of Emergency Medical Aid imeni I. I. Dzhanelidze]

[Abstract] Combined and multiple trauma with shock frequently involves severe purulent-septic complications which are quite difficult to treat. Hemosorption on carbon is used as a detoxication method, but is always accompanied by a decrease in the number of erythrocytes and by hemorrhagic diathesis. The authors have used hemosorption by extracorporal connection of a pig spleen, developed at the Scientific Research Institute of Transplantology and Artificial Organs. The method was used clinically on 20 patients with severe combined trauma complicated by shock and purulent-septic processes, including 12 with sepsis confirmed by bacterial studies. The clinical effects of detoxification included clear improvement of physical and psychoemotional state, return of appetite, and disappearance of fever; these effects lasted for 2-3 days after treatment. Treatment was repeated as many as five times in some cases. Biochemical and laboratory studies confirm the clinically obvious improvement of the patients. This first clinical experiment of the use of hemosorption by extracorporal connection of xenospleen indicates the great effectiveness of this method, resulting from the sorption and immunomodulating effect of the pig spleen. References 9: 7 Russian, 2 Western.

Early Diagnosis of Cardiovascular Disease By Expert Systems on Personal Computers
18400508c Moscow KARDIOLOGII in Russian Vol 28 No 6, Jun 88 (manuscript received 16 Sep 87) pp 104-106

[Article by F. V. Ballyuzek, Ye. V. Dobrynin, M. I. Polyakov, E. R. Useinov, N. A. Gordeyev and Ye. M. Trunin, Cardiosurgery Department, Central Scientific Research Laboratory, First Leningrad Medical Institute imeni I. P. Pavlov, Department of Surgical Diseases, Leningrad Sanitary-Hygiene Medical Institute]

[Abstract] A two-stage screening process was used on some 8,000 workers at a large scientific-production association in Leningrad. The first stage involved processing the data from medical history interviews. The second stage involved the use of an expert system with artificial intelligence features running on personal computers. The researchers used an Iskra-226 microcomputer. The expert system was intended to model the rules for logical deduction to be used by a cardiologist to identify further measures for a given contingent of patients. The system enabled determination of the health of large numbers of persons; considerable refinement of notions concerning the morbidity due to the major cardiologic and angiocardiosurgical diseases, including their preclinical stages; demonstration of the possibility of utilizing specialists of various professional levels, including senior students, without reducing the quality of medical treatment. Reference 1: Russian.

UDC 577.218:577.175.1.14.02

Induction of PR-Proteins by Endogenous Cytokinins in Transgenic Nicotiana Tabacum Plants

18400016b Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 301 No 3, Jul 88 (manuscript received 7 Apr 88) pp 743-745

[Article by V. M. Zakharyev, A. Sh. Tashpulatov, K. M. Nurkiyanova, M. E. Talyanskiy, I. B. Kaplan, I. G. Atabekov, corresponding member, USSR Academy of Sciences, and K. G. Skryabin, Institute of Molecular Biology, USSR Academy of Sciences, Moscow; Moscow State University imeni M. V. Lomonosov; Institute of Bioorganic Chemistry, Uzbek SSR Academy of Sciences, Tashkent]

[Abstract] A study was conducted on the regulation of PR-proteins (patho-genesis related) in transgenic Nicotiana tabacum plants to assess the role of cytokinins in plant resistance to viruses. T. tabacum var. Petit Havana SR1 plants were transformed with an agrobacterium bearing plasmid vector Bin 19 carrying the isopentenyl transferase gene, an enzyme involved in the synthesis of cytokinins. Regeneration of plants from the leaf disks resulted in specimens producing PR-proteins, whereas plants failing to express isopentenyl transferase activity did not form PR-proteins. The data were consistent with the interpretation that enhanced synthesis of cytokinins induced the synthesis of the PR-proteins in T. nicotiana. In addition, infection of the latter plants with TMV resulted in much lower yields of the virus than in control plants. However, a final determination of the contribution of the PR-proteins to viral resistance in this case remains as yet elusive in view of the fact that the transformed plants show considerable morphologic deviation from control plants. Nevertheless, the demonstration that cytokinins are directly related to PR-protein synthesis opens new avenues in research on viral resistance of transgenic plants. Figures 3; figures 11: 1 Russian, 10 Western.

UDC 591.4:613.168

Structure of Internal Animal Organs in Short-Term Exposure to Commercial-Frequency Electromagnetic Field

18400503 Kiev VRACHEBNOYE DELO in Russian No 5, May 88 (manuscript received 30 Nov 87) pp 93-94

[Article by I. P. Kozyarin, Department of Hygiene, Kiev Medical Institute]

[Abstract] The goal of this work was to evaluate the effect of an electromagnetic field of commercial frequency on structural and functional changes at cellular, tissue, and organ levels of white male rats exposed for 2 hours daily (test series I) to magnetic fields with intensities of 1, 2, 4, 7, and 15 kW/m and for 0.5 hour daily (series II) at 7, 12, and 15 kW/m. The changes in organ structure observed related to the duration of exposure and to the intensity of the magnetic field. The morphological changes were similar in all the animals, although some were more severe at the higher field intensities. The rats exposed to intensities of 7-15 kW/m showed vascular disorders (plethora) and moderate dystrophic changes in the brain and the internal organs.

UDC 547.967.4:612.81

Antinarcotic and Antialcohol Effects and Prospects for Clinical Application of Neurohypophyseal Hormones

18400459 Riga IZVESTIYA AKADEMII NAUK LATVIYSKOY SSR in Russian No 5, May 88 pp 43-54

[Article by O. S. Papsuyevich and G. I. Chipens, Institute of Organic Synthesis, Academy of Sciences of the Latvian SSR; published under the rubric "Scientific Reviews"]

[Text] Since the discovery in the mid-1970's of the multifaceted effects of neuropeptides on central nervous system (CNS) function, including mental, a new chapter of intensive study of their biological properties has been opened for many previously well-known peptide hormones and kinins. Most attention has been given to the neurohypophyseal hormones (NHH) vasopressin, oxytocin, vasotocin and others. Of course, vasopressin has pronounced antidiuretic and vasopressor activity and, due to these fundamental hormonal properties, participates in the regulation of the water-salt balance and hemodynamics of the body. Oxytocin has a contractile effect on the smooth muscles of the uterus and the myoepithelial cells of the mammary gland, thus participating in the fertilization and reproductive processes.

Over the last 10 to 15 years numerous effects of NHH on CNS function have been discovered. Vasopressin has been shown to participate in the regulation of memory and learning processes [1-6], sleep and wakefulness [7,8], pain sensations [9,10], thermal regulation [11], immune homeostasis and environmental adaptation [12-14]. These biological properties open prospects for using NHH in the treatment of neurologic and psychiatric conditions. Vasopressin is already being used by clinicians as an effective drug for amnesia [15,16] and several other diseases and dysfunctions of higher nervous activity [17,18].

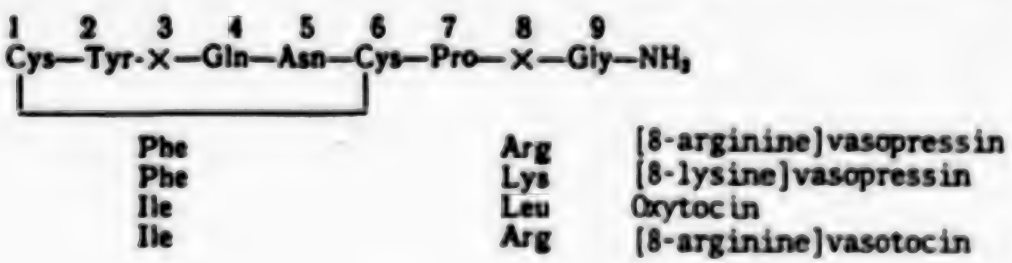
Recent years have seen a great expansion of the volume of experimental work devoted to the study of NHH effects on the development of tolerance to narcotic substances and alcohol and of physical dependency on these drugs and to studies of the antinarcotic and antialcohol NHH properties. The exacerbation in past years of the problem of drunkenness and alcoholism has endowed these studies with renewed urgency. The resolution of the Central Committee of the CPSU of 7 May 1985, "On Measures Aimed at Overcoming Drunkenness and Alcoholism," notes that "special importance is attached to strict compliance with the principles of communist morals and ethics and the overcoming of noxious habits and remnants of the past, above all, the ugly phenomena of drunkenness and alcohol abuse.[1] Alcohol abuse has an extremely negative effect on people's health and the economy. Appropriate measures have been taken to overcome these negative phenomena; the Presidium of the Supreme Soviet of the USSR on 16 May 1985 issued the decree "On Intensifying the Fight Against Drunkenness,"[2] and the Presidium of the Supreme Soviet of the Latvian SSR on 24 May 1985 promulgated the decree "On Measures for Intensifying the Fight Against Drunkenness and Alcoholism and for Eradicating Moonshine Brewing."[3] In a comprehensive alcoholism prevention and treatment program major importance is attached to the medical-biological aspects of the problem.

The present paper summarizes the published data on the antinarcotic and antialcohol properties of NHH and evaluates their potential uses in the treatment of chronic alcoholics.

Of the 11 NHH discovered up to now, two substances—[8-arginine]vasopressin and oxytocin—are hormones naturally occurring in most mammals and man, with well-studied endocrine properties. They are produced by hypothalamus nuclei as high-molecular-weight precursors (propressophysin and prooxyphysin), which are released by proteolysis and accumulate in the posterior hypophysis lobe (neurohypophysis). In the pig and related animals [8-lysine]vasopressin is formed instead of [8-arginine]vasopressin. In the mammalian epiphysis an NHH of lower vertebrates ([8-arginine]vasotocin) has also been discovered, but its function has not been reliably determined.

Since tolerance to drugs and alcohol and the physical dependency on them have similarities and probably share certain biochemical mechanisms with learning and memory processes, it is relevant to begin with a brief outline of NHH effects on these processes.

The most characteristic NHH effect on higher nervous activity is that these substances modulate learning and memory processes [1-5]. As early as the 1960's a group of



Dutch investigators led by de Wied showed that vasopressin promotes a faster development of certain conditioned reflexes in animals and noticeably slows down the subsequent loss of these reflexes[19]. Effective neuropeptide doses for systemic administration to rats are 0.1-10 µg; for intracerebral administration, 0.025-2.5 ng. Vasopressin participation in memory processes was confirmed experimentally by classical endocrinological studies with removal of the glands studied and introduction of an exogenous hormone secreted by the gland. In hypophysectomized rats vasopressin injection restored the capacity for developing and retaining defensive conditioned reflexes that had rapidly deteriorated after hypophysectomy. The importance of NHH to memory-related processes has been demonstrated by studies on animals incapable of endogenous vasopressin production, such as homozygotic Brattleboro rats with hereditary diabetes insipidus. The animals exhibit a markedly weakened capacity for developing and, especially, retaining conditioned reflexes of active and passive avoidance[20]. Immediately or shortly after developing passive avoidance, the animals still retain their response, but after 24 hours are subject to profound amnesia. Similar memory dysfunctions are observed in normal animals after injection of vasopressin-specific antiserum into brain ventricles.

Administration of large oxytocin doses (subcutaneously or intraperitoneally) also enhances the stability of conditioned avoidance response in animals, although less effectively than vasopressin. In smaller doses (0.1-1 ng), regardless of the method of administration, oxytocin weakens a preexisting avoidance response, exhibiting an effect opposite that of vasopressin. It is possible that oxytocin is an endogenous amnesic neuropeptide[21]. A weakening of memory by oxytocin has also been observed in humans[22].

Vasopressin improves the reproduction of information stored in the brain as well as accelerating the development of conditioned reflexes and strengthening (consolidating) temporal connections. Experimental amnesia models in rats are often used to study vasopressin's effect on reproduction of conditioned reflexes. Vasopressin and its many analogues and fragments effectively prevent and eliminate retrograde amnesia caused by electric shock, carbon dioxide, antibiotics (puromycin and anisomycin) and other agents.

Arginine-vasotocin also promotes learning and memory dynamics, but its action is definitely weaker than that of vasopressin.

Interestingly, NHH effect on learning processes is affected by the sex of the animal as well as other factors (dosage, method of administration, etc.). The neuropeptide has been found to help learning in males more so than in females. A similar sex correlation for neuropeptide activity has also been observed in humans[23]. Recently, vasopressin analogues were found to affect differently the learning and memory processes in different animal models[24].

NHH has a considerable effect on memory processes in lower vertebrates and insects as well as mammals. Importantly, the general patterns of these effects are similar in man and animals of various phylogenetic levels.

NHH exerts important and multiple effects on learning and memory, but in strength and direction these effects are substantially affected by the dosage and method of administration, the age and sex of the animal or human subject, the condition of the body, the test system and several other factors.

As has been mentioned above, NHH effect on memory and learning bears a considerable resemblance to their effect on tolerance and drug and alcohol dependency, which is probably due to analogies in the underlying physiological and biochemical processes. Both memory processes and drug tolerance/dependency are characterized by specific development, consolidation and extinction rates[25]. When learning sessions are resumed or drugs or alcohol are administered, attenuated or extinct processes (effects) can rapidly be recovered, in a shorter period than the initial development[26]. Local cerebral lesions, protein synthesis inhibitors[27,28], modified activity of neuromediators in the brain, electroconvulsive shock and cortical stimulation[29] exert similar effects on memory and morphine tolerance.

The existing hypotheses attribute tolerance to neurochemical and/or neurophysiological modifications caused by the pharmaceutical substance (drug), which subsequently attenuates the effect of additional doses of the same substance[30]. According to an alternative model based on I. P. Pavlov's theory of conditioned reflexes, an important role in the development of tolerance belongs to stress caused by external stimuli. Such stimuli, which accompany the administration of any pharmaceutical substance, function as the conditional stimulus, while the drug itself functions as the unconditional stimulus[31]. The two hypotheses are not mutually exclusive, so that tolerance is currently considered to be the result of the collective action of these processes.

The development of a tolerance to a drug's action on the CNS is often interpreted as a special kind of learning[31,32]. Memory processes may play a part in developing and maintaining tolerance[49], although this hypothesis needs experimental confirmation. At any rate, numerous data suggest that memory-affecting neuropeptides modulate certain general adaptational processes in a body exposed chronically to narcotic substances[33,34].

Although most investigators believe that alcohol tolerance and physical dependency evolve in an interrelationship and more or less in parallel, a hypothesis has been advanced that they are based on different molecular mechanisms[35].

Moore[36] has shown that arginine-vasopressin in systemic administration (a dose of 100 μg/kg) helps maintain tolerance to the analgesic action of morphine in rats while affecting neither the rate nor the degree of its development. Earlier, other investigators[37] working with unusually large doses found that an analogue of lysine-vasopressin—des-9-glycinamide-[8-lysine]vasopressin (DGA-LVP)—also facilitates morphine tolerance. Similar results were obtained by van Ree and de Wied[38], who studied the development of morphine tolerance in rats administered des-9-glycinamide-[8-arginine]vasopressin (DGA-AVP) and its C-terminal tripeptide Pro-Arg-Gly-NH2. Conversely, the administration of vasopressin antiserum inhibits the process[39]. The modulating effect on drug tolerance by DGA-AVP, DGA-LVP and other vasopressin analogues whose principal hormonal effects are absent or severely attenuated suggests a direct influence of vasopressin on CNS function. It should be noted, however, that vasopressin and its analogues have no affinity for opiate brain receptors and do not inhibit morphine binding with brain receptors[40].

Unlike vasopressin and its analogues, oxytocin facilitates the loss of acquired conditioned reflexes, weakens the development of acute and chronic tolerance, and facilitates the development of physical dependency on narcotic substances (morphine and heroin)[41,42]. A single oxytocin injection shortly before the first session of heroin analgesia effectively prevents tolerance to the drug for three days; this fact is solid proof of the sensitivity to the neuropeptide of the early, developing tolerance phase. Oxytocin has a similar effect when introduced just prior to the last injection of the drug, indicating that oxytocin can also attenuate a predeveloped tolerance.

NHH and their analogues also strongly modulate the self-administration of drugs by animals. Studies in rats showed that vasopressin and its fragments in subcutaneous injections reduce considerably the number of self-administration acts and doses of heroin. On the other hand, oxytocin and intracerebral injections of vasopressin-specific antiserum increased the heroin self-administration rate[43]. NHH thus participate functionally in the development, maintenance or attenuation of a behavior. These and other data, mentioned earlier, suggest that peptides of the vasopressin series can be used for purposeful design and synthesis of highly active prolonged-action analogues as a basis for developing new and effective remedies for drug addiction.

We should point out, however, that the effects of NHH on tolerance to drugs and physical dependency have not been studied sufficiently[44]. Research has been reported, for example[45], where the investigators were unable to detect an influence of vasopressin or oxytocin on tolerance to morphine and arrived at the erroneous conclusion that the role of NHH as endogenous modulators of opioid action is minimal or insignificant.

Several studies[46-50] in rats and mice showed that arginine- and lysine-vasopressins help maintain functional tolerance to the sedative-hypnotic effect of ethanol, while alcohol tolerance gradually disappeared in animals not treated with these neuropeptides. The optimal vasopressin dose in mice with subcutaneous administration was 400 nM/kg of body weight. The neuropeptide activity was also observed with doses smaller by an order of magnitude: 40 nM/kg[49]. Arginine-vasopressin maintained ethanol tolerance for 9-15 days after alcohol was discontinued. A similar effect on tolerance to the hypnotic action of ethanol was produced by intracerebral administration of arginine-vasopressin (1 ng/mouse)[51].

Maintenance of ethanol tolerance was also promoted by vasopressin analogues and fragments, primarily DGA-AVP and DGA-LVP, which exhibit a highly limited hormonal activity[34,49,52]. In first studies of this aspect[53,54] intact and falsely operated rats given DGA-LVP could sustain higher concentrations of ethanol in water solutions than control animals that did not receive the neuropeptide. By contrast, hypophysectomized rats took virtually no ethanol, and this behavior was not changed by peptide administration. The pronounced modulating effect on morphine and ethanol tolerance of endocrinologically inactive analogues and the similar effects of vasopressin administered systemically or intracerebrally indicate the direct action of the neuropeptides on the CNS.

Besides increasing ethanol consumption and maintaining ethanol tolerance, peptides of the vasopressin series facilitate the development of physical alcohol dependency. A continuous infusion of DGA-AVP to mice during the entire period when alcohol dependency was developing in the animals exacerbated convulsions after ethanol was discontinued. This neuropeptide effect was most pronounced for a dose of 0.08 μg/kg[34]. DGA-AVP also tended to exacerbate convulsions after ethanol discontinuation after subcutaneous administration (several times in a dose of 10 μg/mouse). It has been demonstrated that these effects were not due to any subconvulsive activity of DGA-AVP or any change of ethanol blood concentration.

Arginine-vasopressin, lysine-vasopressin and DGA-LVP slow down the extinction of functional tolerance to the ataxic action of ethanol[55]. In that case, however, ethanol tolerance in rats given vasopressin or its analogue disappeared gradually within five days, and even when peptide injections were continued the animals lost tolerance by the seventh day. An unexpected result was obtained with DGA-AVP in this test: the arginine-vasopressin analogue turned out to be inactive, although, as mentioned earlier, it is highly active in maintaining tolerance to the hypnotic action of ethanol. No satisfactory explanation for this phenomenon has been offered.

Tolerance to hypothermic ethanol effect and acute alcohol intoxication is affected by vasopressin and its desglycine analogues weakly and for a brief period of time;

the effect usually disappears the day after ethanol is discontinued[34,56]. After discontinuation of DGA-AVP ethanol tolerance maintained by the drug disappears rapidly.

Hoffman et al.[47,49] showed that oxytocin and arginine-vasotocin do not affect ethanol tolerance. Newer studies by other authors[57], however, have indicated that oxytocin and its C-terminal tripeptide Pro-Leu-Gly-NH_2 (PLG) administered subcutaneously to rats (at 800 nM/kg) slowed down the development of tolerance to the hypnotic action of ethanol. In addition, PLG weakens tolerance also to the hypothermic effect of ethanol in acute intoxication. Tolerance develops in that case by the fifth day after peptide administration. The hypnotic action of ethanol in acute intoxication is not affected by either oxytocin or PLG.

The specific actions of various natural NHH on tolerance and memory processes are apparently not determined by a difference in their distribution throughout the body or metabolism in systemic administration, although these factors may exert some influence; more likely, they are results of the interaction of NHH with specific CNS receptors[48,49]. This is supported by dose-response curves and studies of the correlations between the structures and functions of natural NHH and their structural analogues.

A distinct correlation is observed between NHH structure and the influence on tolerance to the hypnotic action of ethanol. The modulating influence of NHH on ethanol tolerance and self-administration of heroin, as well as on learning and memory processes, is associated mainly with the structure of the cyclic part of the molecule. The main structural elements responsible for these properties of the peptides are two aromatic amino acids in the cyclic part of the molecule: tyrosine and phenylalanine. If even one of these is replaced by an aliphatic amino acid (for example, isoleucine) or any other nonaromatic amino acid, the biological activity of the NHH is drastically changed. Thus, arginine-vasopressin with isoleucine in the cyclic part of the molecule (in the 3-position) cannot maintain ethanol tolerance[49] and has a very slight facilitating effect on learning and memory[1,3,58]. Furthermore, oxytocin with isoleucine in the 3-position and a second aliphatic (neutral) amino acid—leucine—in the 8-position, in contrast to vasopressin, slows down both the development of conditioned reflexes and the development of tolerance to drugs and alcohol.

Unlike the cyclic part of the molecule, linear C-terminal fragments (di-and tripeptides) of vasopressin and oxytocin, which have a pronounced activity for prevention and elimination of retrograde amnesia, have no effect or a slight effect on the loss of conditioned defensive reflex of avoidance and on alcohol tolerance, while facilitating the development of morphine dependency. The C-terminal tripeptide of oxytocin is the neuropeptide structure responsible for facilitating the self-administration of heroin[43]. Interesting results have been obtained in studies of derivatives of C-terminal fragments of oxytocin. In particular, the N^{α}-benzyloxycarbonyl derivative Pro-Leu-Gly-NH_2 has no significant effect on ethanol tolerance in mice. In an experimental test involving amnesia caused by puromycin, however, the substance exhibited an even stronger activity than did arginine-vasopressin. Another modified oxytocin fragment—the cyclic dipeptide Leu-Gly—was active in an ethanol tolerance maintenance test, but its dose (4 μM/kg) was larger by an order of magnitude than that of arginine- or lysine-vasopressin[49].

It is now generally acknowledged that various neuromediator systems of the brain take part in the mechanisms responsible for the emotiogenic effect of ethanol and development of a craving for it. Ethanol sharply intensifies the synthesis and secretion of the catecholamines norepinephrine and dopamine into the synaptic gap[59,60]. For example, in ethanol-preferring rats dopamine content in the brain is 15-25 percent higher than in water-preferring animals. This change in brain catecholamine content correlates well with the development of subjective sensations in humans and behavioral responses in animals after one-time ethanol administration and in chronic alcoholization. A dopamine excess in the brain coincides with severe withdrawal symptoms. It has been suggested that the leading role in the development and maintenance of ethanol craving is played by α-receptors of the noradrenergic system. In the physical dependency stage, the role of the noradrenergic system in alcohol craving becomes reduced as dopaminergic mechanisms get involved in the process[61]. Correction of ethanol-induced dysfunction in these neuromediator systems with the aid of specific modulators (such as many of the neuropeptides, including NHH) thus appears to be a promising approach to the prevention and treatment of alcoholism.

Hoffman et al.[62] have shown that the noradrenergic system of the brain must be intact in order to maintain tolerance to the hypnotic action of ethanol with arginine-vasopressin. When it is destroyed or disconnected the neuropeptide has no effect. Since arginine-vasopressin itself does not affect ethanol sensitivity in animals, alcohol tolerance is apparently maintained via modulation by the vasopressin of noradrenergic and possibly dopaminergic neuronal activity in the CNS. This is supported by studies of the important role of the noradrenergic system in retention of the conditioned reflex of passive avoidance response: when noradrenergic neurons of the ascending dorsal bundle are destroyed the influence of vasopressin on the development and retention of the conditioned reflex of avoidance in rats disappears. The noradrenergic system of the brain participates in memory processes[63,64] and is also necessary for developing and maintaining ethanol tolerance[60, 62]. The effect of vasopressin on these processes may be mediated by its modulating action on the synthesis and release of catecholamines in the brain. Vasopressin injections, in contrast to ethanol, are known to reduce the

norepinephrine and dopamine content in the hypothalamus, hippocampus, midbrain, parietes, and striated body. The modulation of the activity catecholaminergic and, in particular, noradrenergic neurons by vasopressin may affect the development and manifestation of tolerance not only to ethanol but also to other sedative-hypnotic substances, such as phenobarbital[62].

Serotoninergic brain systems also participate in the mechanisms of NHH action on memory and ethanol tolerance processes. The structures responsible for tolerance are the raphe nuclei and mesolimbic serotoninergic pathways[65]. Administration of vasopressin or DGA-AVP helps maintain tolerance to hypothermic and ataxic ethanol effects in animals only if the raphe nuclei are intact. If they are destroyed by 5,6-dihydroxytryptophan, 6-hydroxydopamine or electric coagulation, the effect of vasopressin on the retention of conditioned avoidance reflex is blocked[66,67], no tolerance to ethanol develops[68] and vasopressin has no effect on maintaining tolerance to ethanol[69]. Several hypotheses have been advanced to account for the absence of vasopressin effect on tolerance to ethanol when raphe nuclei are destroyed. The most probable hypothesis suggests that DGA-AVP maintains tolerance by affecting mesolimbic serotoninergic conducting pathways, executing pre-or postsynaptic action, either directly on raphe neurons or on their hippocampal neuronal targets[69].

It is still unclear whether endogenous vasopressin plays a part in the development and expression of ethanol tolerance. However, ample clinical data have been accumulated indicating a lower vasopressin level in the blood plasma of drug addicts and alcoholics and a reduced vasopressin concentration in the brain in patients developing physical ethanol dependency. Interestingly, for a brief period directly after systemic introduction of ethanol animals exhibited a slight rise of vasopressin level in blood plasma[70]. This is apparently due to the stress factor associated with acute ethanol administration.

The molecular mechanisms responsible for the drop in brain vasopressin concentration caused by ethanol have not been studied. It has been hypothesized that the causes could include either an enhanced activity of proteolytic enzymes that split vasopressin or an inhibitory action of ethanol upon the normal secretion of vasopressin, which, collectively with other factors, disrupts metabolic processes in alcoholics[71]. An alternative hypothesis is that ethanol and vasopressin are antagonists. It is possible that a vasopressin deficit and an excess of dopamine in the brain are among the causes of the withdrawal syndrome in physical ethanol dependency.

Thanks to the pronounced stimulative effect in the development and retention of conditioned reflexes and long-term memory, vasopressin is already being used successfully for clinical treatment in conditioned reflex therapy of chronic alcoholics. Using drugs that produce nausea and emetic responses when combined with alcohol (i.e., the development of a negative conditioned reflex to alcohol consumption) was suggested by V. M. Bekhterev and later explained and elaborated by I. P. Pavlov and his disciples in terms of the theory of conditioned reflexes. The drug of choice for conditioned reflex therapy in chronic alcoholics is apomorphine, which affects selectively the emesis center and causes vomiting[74]. In order to intensify an emetic response which is elicited not only by the taste and smell of alcoholic beverages but even by their mental image, apomorphine is combined with strychnine, thiolic preparations and hypnotic suggestion therapy[75,76]. The conditioned reflex, however, is often insufficiently strong and the negative motivation against alcohol becomes inoperative for the patient. Moreover, apomorphine treatment is limited by side effects (collapse, hemorrhages in the stomach and the cardial section of the esophagus and convulsive fits) and contraindications (bronchial asthma, peptic/duodenal ulcer and hypertension).

In order to retain and reinforce the negative conditioned reflex to alcohol while reducing side effects and narrowing the range of contraindications to apomorphine, G. V. Morozov, A. M. Ivanitskiy, et al.[71,77,78] have used [8-lysine]vasopressin. They showed that in an experimental group with apomorphine and vasopressin the negative conditioned reflex to ethanol was developed in 79 percent of the patients but in just 14 percent of patients in the control group, where only apomorphine was used. The conditioned reflex to apomorphine in the patients who received lysine-vasopressin was stronger by a factor of 1.5 than in the control group. A follow-up study a year after the treatment showed that 50 percent of patients receiving lysine-vasopressin abstained from alcohol and were in good health and actively employed. In the control group only 14 percent of the patients reported that they abstained from alcohol[77,78].

This effective action of vasopressin combined with apomorphine in the treatment of chronic alcoholics can be explained by the interaction of two basic mechanisms: the synergistic action of the drug and the neuropeptide upon the catecholaminergic brain systems, particularly the dopaminergic system, and the specific action of vasopressin on memory, which facilitated the fixation of neurochemical and behavioral changes induced by the drug treatment[77].

Clinical uses of [8-arginine]vasopressin in the treatment of chronic alcoholics have not been described in the literature. However, numerous comparative studies of psychopharmacologic properties in animals have shown this drug to have a stronger activity than lysine-vasopressin. These data and successful use of arginine-vasopressin in the clinical treatment of amnesia and other diseases and dysfunctions of higher nervous activity suggest that this neuropeptide must be effective for treatment of chronic alcoholics.

In summary, it can be said that the combination of vasopressin's antiamnesic[1,4,40], antidepressive[72] and adaptogenic[73] psychopharmacologic properties, its stimulation of learning and memory[1-4] and its antagonism to sedative-hypnotic and ataxic actions of ethanol suggest that neuropeptides of the vasopressin group, and especially endocrinologically inactive analogues, have strong indications recommending them for use to correct acute alcohol intoxication and certain other alcohol-induced conditions and for comprehensive treatment of patients suffering from chronic alcoholism.

Footnotes

1. PRAVDA, 17 May 1985.

2. PRAVDA, 17 May 1985.

3. SOVETSKAYA LATVIYA, 25 May 1985.

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Biological Foundations of the Search for Agents for Differential Anti-Alcoholism Pharmacotherapy

18400494a Moscow VESTNIK AKADEMII MEDITSINSKIKH NAUK SSSR in Russian
No 3, Mar 88 (manuscript received 29 Jun 87) pp 28-32

[Article by A. V. Valdman, A. I. Mayskiy, A. B. Kampov-Polevoy, V. G.Treskov and E. S. Drozdov, Scientific Research Institute of Pharmacology, USSR Academy of Medical Sciences, Moscow]

[Abstract] Experiments on mice and rats have demonstrated that there are different levels and types of natural inclination toward consumption of alcohol. Passive animals with a natural tendency to consume large quantities of alcohol show a reaction to certain alcoholism-control medications that is opposite that of active animals with less of a tendency toward alcohol abuse. Analysis of background levels of stress hormones such as ACTH and closely related neuropeptides have shown clear differences among human patients with different forms of alcoholism. Selection of individual pharmacotherapy for alcoholism must involve analysis of the clinical pharmacokinetics of the various preparations available utilizing modern effector models. The use of the differentiated pharmacotherapy for alcoholism patients has been adapted for use in drug-treatment centers associated with industrial enterprises. The differentiated approach to pharmacotherapy of alcoholism has resulted in 25 percent fewer violations of sobriety among patients than with the traditional approach, leading to a four to seven percent increase in worker output. References 10: 8 Russian, 2 Western.

Biochemical Approaches for Eliminating the Craving for Alcohol

18400494b Moscow VESTNIK AKADEMII MEDITSINSKIKH NAUK SSSR in Russian No 3, Mar 88 (manuscript received 29 Jun 87) pp 40-43

[Article by Yu. S. Borodkin, Institute of Experimental Medicine, USSR Academy of Medical Sciences, Leningrad]

[Abstract] There are at present no biological agents for the prevention of alcoholism, because of the lack of reliable diagnostic criteria and information on the pathogenic mechanisms predisposing animals and man to the consumption of alcohol. A radical solution to the treatment of alcoholism requires determination of the molecular and biological mechanisms forming the basis of the predisposition to consumption of alcohol and pathologic craving for it, as well as determination of the disorders of biochemical mechanisms caused by acute and chronic alcohol intoxication. The authors conclude that there is a promising means for preventing alcoholism in the stage of the formation of the craving for alcohol, by effective utilization of pharmacologic agents which not only decrease consumption of alcohol, but also provide a stress-protective effect. Central α-adrenergic blockers such as phenoxybenzamine and nootropic compounds such as ethimizol were found to decrease the consumption of ethanol by rats by 40-50 percent when administered over a period of 6-12 days and were effective in the stage of the formation of the craving for ethanol. References 11: 8 Russian, 3 Western.

Effect of Cholinesterase Inhibitors on Nociceptive Stimulation in the Spinal Cord

18400495A Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 51 No 3, May-Jun 88 (manuscript received 7 Apr 87) pp 12-14

[Article by A. Yu. Nemirovskiy, Department of Pharmacology, Therapeutic and Sanitary-Hygiene Faculties, First Moscow Medical Institute imeni I. M. Sechenov]

[Abstract] A study is made of the effect of the cholinesterase inhibitors physostigmine and galanthamine on the transmission of nociceptive information in the afferent paths of the spinal column. Experiments were performed on white rats to determine the effect of the two substances on spontaneous bioelectric activity and activity evoked by intraarterial administration of bradykinin. In contrast to m-cholinomimetics, the cholinesterase inhibitors studied increased both spontaneous and bradykinin-evoked bioelectrical activity when administered intravenously. Atropine intensifies this effect. In a second series of experiments, the preparations were administered through an intrathecal catheter, so that they reached the lower thoracic and upper lumbar segments innervating the posterior extremities. Five minutes after intrathecal administration of physostigmine at 1 μg, spontaneous activity decreased by 13 percent. The bradykinin reaction decreased by 17 percent. Greater doses had greater depressing influence on bioelectric activity. Galanthamine had a similar effect. Atropine eliminated the depressing effect of the cholinesterase inhibitors on bradykinin-induced bioelectrical activity. References 10: 1 Russian, 9 Western.

Relationship Between Choline-Blocking and Protective Effects of M-Cholinolytics In Chlorophos Poisoning

18400495B Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 51 No 3, May-Jun 88 (manuscript received 25 Dec 86) pp 25-27

[Article by A. B. Kosmachev, V. V. Petrov and S. M. Chigareva, Institute of Toxicology, USSR Ministry of Public Health, Leningrad]

[Abstract] Selective peripheral m-cholinolytics are used to study the relationship between the choline-blocking effects and the protective effects of preparations in organophosphorus poisoning. Experiments were performed on white mice. The peripheral m-cholinolytics atropine iodomethylate and methacine were administered subcutaneously in various doses 30 minutes before testing, and their cholinomimetic antagonism was determined. The threshold doses of peripheral cholinolytics at which the compounds have no central effect were determined: 16 mg/kg for methacine, 4 mg/kg for atropine iodomethylate. A direct proportional dependence was found between the choline-blocking and protective effects of the chlorophos and exogenous acetyl choline used to poison the mice. For acetyl choline poisoning, the protective effect is independent of the cholinolytic used, varying only with the degree of m-cholinoreceptor blockage. Atropine iodomethylate has a stronger selective peripheral m-cholinolytic effect than methacine. Figure 1, references 3: 1 Russian, 2 Western.

Mathematical Modeling in Predicting Drug Effects

18400463b Moscow ZNANIYE-SILA in Russian No 6, Jun 88 p 17

[Unattributed report: "Taking a Sublingual Tablet..."]

[Text] How often it is that we have to do just that in our everyday life! And what is important is that once having taken a Validol tablet, we feel so much better. The mechanism of this drug's cardiotropic action is not that overbearing any longer, although it is rather complex. According to associates at the USSR Ministry of the Medical and Biological Industry Scientific-Research Institute for the Biological Testing of Chemical Compounds and the USSR Academy of Sciences Control Problems Institute, the underlying mechanism is the ionic effect on heart muscle cells exerted by the physiologically active substances that go into medicinal preparations. When pharmacologists synthesize new preparations, they must perform a great many tests on laboratory animals in order to achieve, in the first place, the maximum effect of the drug on the heart and, in the

second place, a minimum of undesirable accumulation of the test drug in other organs and tissues. How can this trial and error procedure be shortened?

Scientists have taken advantage of mathematical modeling. The initial data for the model are taken from experiments on laboratory rats. Then a measurement is made of the heart's contractile and electrical response to the drug Diltiazem, a substance with a recognized therapeutic action. Modeling of the entire process identified the drug's mechanism in the following way: The concentration of free calcium ions in the region surrounding the heart muscle cell directly affected cardiac activity. The role of the drug essentially boiled down to regulating the flow of these ions. Consequently, the cardiotropic effect of each new preparation can in principle be predicted by a computerized evaluation of the drug's ability to intensify or attenuate calcium content in the region, thereby significantly reducing the necessity of lengthy and costly animal experimentation.

UDC 582.287:547.751

Psilocybin-Containing Fungi of the USSR Studied

18400497a Leningrad MIKOLOGIYA I FITOPATOLOGIYA in Russian Vol 22 No 2, Mar-Apr 88 pp 120-122

[Article by A. M. Bekker, L. S. Gurevich, T. N. Drozdova, A. I. Ivanov, and N. V. Belova, USSR Academy of Sciences Botanical Institute imeni V. L. Komarov, Leningrad, under heading "Physiology and Biochemistry of Fungi": "Search for Psilocybin-Containing Agaric Fungi in the Territory of the USSR"]

[Text] Over the course of the last 30 years intensive studies have been going on on basidiomycetes of the order Agaricales, which possess hallucinogenic properties. Of particular interest are the species which contain the pharmacologically active indol compound psilocybin. At the present time approximately 120 species of Agaricales fungi are known, approximately half of which produce psilocybin (Bekker et al., 1985). This compound is found in the fruiting bodies of representatives of seven families and 11 genera: the families Bolbitiaceae (genera Agrocybe, Conocybe), Coprinaceae (genera Copelandia, Panaeolus, Psathyrella), Cortinariaceae (genera Gymnopilus, Inocybe), Hygrophoraceae (genus Hygrocybe), Plueaceae (genus Pluteus), Strophariaceae (genus Psilocybe), Tricholomataceae (genus Gerronema) (Bekker et al., 1985; Stijve, Kuyper, 1985, and others). The greatest number of psilocybin-containing species (about 30) belongs to the genus Psilocybe (Guzman, 1983; Bekker et al., 1985).

Investigation of psilocybin-containing basidiomycetes was begun and most completely carried out in Mexico and Central America, which are the genocenter of origin of the hallucinogenic fungi of the genus Psilocybe. Subsequently, analogous works were done in North America (United States, Canada), Western Europe (Great Britain, GDR, Italy, Norway, Czechoslovakia, Finland, and others); there is fragmentary information on the mycoflora of Australia; data on Africa and Asia (apart from Japan) is practically nonexistent (Heim, Wasson, 1958; Guzman, 1983; Bekker et al., 1985, and others). In the USSR as well, no studies have been done on this genus.

This work cites data on the discovery of psilocybin-containing species of basidiomycetes in the territory of our country. The main attention is focused on studying species from the families listed above. Besides this, studies have been done on representatives of the family Amanitaceae, since biologically active indol compounds have been found in them which are close in structure to psilocybin (Tyler, 1965, and others). Analysis has been done on 73 samples of fruiting bodies collected in Leningrad (L.O.), Irkutsk (I.O.), Kiev (K.O.), and Penza (P.O.) oblasts, Krasnoyarsk (K.K.) and Altay (A.K.) krays, and the Estonian SSR in 1982-1986. A total of 48 species of fungi have been studied, the majority of which were being studied for the first time: Agrocybe fimicola (Speg.) Sing. (K.K.-1), Amanita muscaria (L:Fr.) Hooker (L.O.-1), A. pantherina (DC.:Fr.) Secr. (L.O.-1), A. porphyria (A. et S.:FFr.) Secr. (L.O.-1), A. Rubescens (Pers.: Fr.) S. F. Gray (L.O.-1), Conocybe semiglobata Kuehner ex Sing. (L.O.-2), Gymnopilus picreus (Pers.: Fr.) Karst (L.O.-1), G. sapineus (Fr.) Maire (L.O.-1), G. Spectabilis (Fr.) Sing. (L.O.-1, P.O.-1, A.K.-1), Panaeolina foenisecii (Pers.: Fr.) Maire (P.O.-1), Panaeolus rickenii Hora (P.O.-1), P. sphinctrinus (Fr.) Quel. (P.O.-1, K.K.-1), Pholiota adiposa (Fr.) Kumm. (L.O.-1), Ph. astragalina (Fr.) Sing. (L.O.-1), Ph. aurivella (Batsch: Fr.) Kumm. (L.O.-1), Ph. carbonaria (Fr.:Fr.) Sing. (P.O.-1), Ph. curvipes (Fr.) Quel. (P.O.-1, A.K.-1), Ph. destruens (Brond.) Gill. (L.O.-3), Ph. Flavide (Schaeff.: Fr.) Sing. (L.O.-1), Ph. flammans (Fr.) Kumm. (L.O.-1), Ph. flammuloides Mos. (A.K.-1), Ph. heteroclita (Fr.) Quel. (L.O.-1), Ph. gummosa (Lasch) Sing. (L.O.-1), Ph. lenta (Pers.:Fr.) Sing. (L.O.-1), Ph. lucifera (Lasch) Quel. (L.O.-6, P.O.-1), Ph. ochropallida Romagn. (L.O.-2), Ph. spumosa (Fr.) Sing. (L.O.-1), Ph. squarrosa (Muller:Fr.) Kumm. (L.O.-1), Ph. tuberculosa (Schaeff.: Fr.) Kumm. (L.O.-9), Pluteus atricapillus (Secr.) Sing. (L.O.-1), Psathyrella cernua (Vahl:Fr.) Mos. (L.O.-2), P. gracilis (Fr.) Quel. (P.O.-1), P. hydrophila (Bull.) Maire (P.O.-1), P. orbitarum (Romagn.) Mos. (L.O.-1), P. sarcocephala (Fr.: Fr.) Sing. (ESSR-1), P. subatrata (Batsch.: Fr.) Gill. (P.O.-1), P. subcernua (Schulz.) Sing. (P.O.-1), Psilocybe montana (Pers.: Fr.) Quel. (L.O.-1), S. albocrenulata (Pk.) Kreisel (L.O.-1), S. coronilla (Bull.: Fr.) Quel. (P.O.-1), S. cyanea (Bolt.) Tuomikoski (ESSR-2), S. inuncta (Fr.) Quel (ESSR-1), S. semiglobata (Batsch: Fr.) Quel. (L.O.-2), S. rugosoannulata Farlow ex Murr. (K.O.-1) Tephrocybe palustris (P.K.) Donk. (L.O.-1).[1]

Analysis of water-alcohol extracts of the specimens was carried out by the method of thin-layer chromatography with standard psilocybin on Silufol plates (15 x 15 cm,

Czechoslovakia) in two eluting systems: butanol-glacial acetic acid-water (2:1:1 or 24:10:10) and n.-propanol-5 percent aqueous ammonia (5:2). Identification was carried out using the Ehrlich reagent, and sensitivity was 0.1 micromole (Hatfield et al., 1978).

In all the specimens studied, with the exception of Psilocybe semilanceata, no psilocybin was found. It should be emphasized that for Panaeolus sphinctrinus, Gymnopilus spectabilis, Pholiota curvipes, Ph. lucifera, and Psilocybe montana, consistent negative results were obtained independent of the geography of collecting the fruiting bodies. For the species Amanita porphyria, Gymnopilus picreus, G. sapineus, Panaeolina foenisecii, Panaeolus rickenii, P. sphinctrinus, Pholiota squarrosa, Psathyrella hydrophila, Psilocybe montana, Stropharia aeruginosa, S. cyanea, S. innucta and S. semiglobata, which were previously studied (Tyler, 1965; Mantle, Waight, 1969, 1969; Fiussello, Scurti, 1972; Hatfield et al., 1978; Koike et al., 1981; Margot, Watling, 1981; Christiansen, Rasmussen, 1983, and others), the negative result which we obtained agrees with the data of other authors.

It is known that the capacity to accumulate psilocybin possessed by a number of representatives of the genera Gymnopilus and Panaeolus cannot be considered a reliable species indicator (Fiussello, Scurti, 1972; Bekker et al., 1985), since it depends on ecological and geographic factors (Hatfield et al., 1978). For example, in the fruiting bodies of Gymnopilus spectabilis collected in Japan, no psilocybin was found (Koike et al., 1981), while analysis of a set of European specimens yielded ambiguous results. Psylocibin was present in only 4 of the 13 specimens (Hatfield et al., 1978). In connection with this, we focused special attention on studying this species. In analyzing the fruiting bodies of G. spectabilis from various regions of the USSR (Altay Kray, Leningrad and Penza oblasts), negative results were obtained. Additional research on the species was carried out under conditions of artificial cultivation: analysis was done on two samples of mycelium accumulated under stable conditions, and four samples of carpophores of G. spectabilis (Strain 0392 of the collection of the USSR Academy of Sciences Botanical Institute). The mycelium was grown in a liquid nutrient medium, and in order to obtain fruiting bodies solid-phase cultivation was used on wood shavings (birch, aspen) moistened with wort [suslo] over the course of 9-10 weeks at 18 degrees C and 100 percent relative humidity. Psilocybin was not found in a single one of the cultivated specimens, which, possibly, is caused by their common origin from a strain isolated in a culture in 1965 from a carpophore found in Leningrad Oblast, and it agrees with the results of analysis of natural fruiting bodies.

Out of all the species studied, only the Psilocybe semilanceata specimen consistently contained psilocybin. This species is widespread in the temperate latitudes, in particular, according to the data of V. A. Urbonas (1978), in regions of the USSR such as the Caucasus, the Far East, the Ukrainian SSR, Estonian SSR, and Leningrad Oblast. Our discovery of psilocybin in the fruiting bodies of P. semilanceata agrees with the data in the literature, which attests that carpophores of this species which come from various geographic origins are consistently characterized by a high concentration of psilocybin—up to 23.7 mg/g dry weight (Mantle, Waight, 1969; Stijve, Kuyper, 1985, and others).

Thus, the screening which was carried out attests that psilocybin-containing species are rare in the territory of the USSR. Further studies, no doubt, should expand the search to the most promising psilocybin-containing genera which grow in our country—Gymnopilus, Inocybe, Panaeolus, and Psilocybe. Taking into account the published data on the ecology of these genera, it is worthwhile to concentrate our attention on the mountainous zones such as the Carpathians, the Caucasus, and the mountainous regions of Central Asia and the Far East.

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Footnotes

1. Figure indicates the number of samples studied.

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Cellular Reception, Transduction and Implementation of External Inputs as Universal Model for Systematic Drug Testing and SAR Analysis

18400016d Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 301 No 3, Jul 88 (manuscript received 20 Apr 88) pp 765-768

[Article by A. I. Luyk, V. P. Kukhar, member, UkrSSR Acad. Sci., L. I. Savranskiy, R. N. Skryma, V. V. Mukhin and V. L. Sheptun, Institute of Bioorganic Chemistry, Ukrainian SSR Academy of Sciences, Kiev; Kiev State University imeni T. H. Shevchenko]

[Abstract] Studies on the involvement of interlukin in the regulation of cell division led to the unexpected results that two structurally unrelated agents—BW 755C and mechlorethamine (embikhin)—yielded virtually identical results in terms of their actions on phospholipase C-based cellular signal system. More detailed studies with both agents led to the proposition that the latter system of cellular input reception, transduction, and implementation of physiological sequelae may serve as a universal drug screening system and for SAR analyses. Systematized data have shown that alpha$_2$-adreno- and M_1-cholinergic agents, as well as Ca^{2+} ionophores, protein kinase C inducers, chemotactic fMZP tripeptide, endogenous bioregulators, and second messengers (leukotrienes, diacylglycerol, 1,4,5-inositol triphosphate), hypoglycemics, etc., function as activators of this system. Agents showing inhibitory effects include alpha-adreno- and M-cholinolytics, alkylating antineoplastic agents, antihistaminics, phenothiazine, and inhibitors of oxidative metabolism of arachidonic acid. Quantum chemical evaluation of the activators and inhibitors with calculation of spatial configuration and molecular orbitals demonstrated that all inhibitors have a pharmacophoric group consisting of three proton acceptor centers. The latter have an effective charge in the -0.12 to -0.3 range and may be displaced to one side of the molecule as a result of configurational lability. The activators, on the other hand, share a more symmetrical disposition of the proton acceptor centers with the same range of effective charges. However, for energetic reasons the proton acceptor moieties cannot be localized at one facet of the molecule. These observations point to the existence of universal parameters that may be used in drug design and screening in conjunction with SAR studies. Figures 1; references 6 (Western).

Cardio- and Hemodynamic Effects of Crown-Ether Derivative and Experimental Analysis of Its Cardiotropic Effect

18400495c Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 51 No 3, May-Jun 88 (manuscript received 30 Jun 87) pp 36-38

[Article by G. B. Kovalev, K. G. Gurbanov, N. G. Lukyanenko and S. S. Basok, Department of Pharmacology, Volgograd Medical Institute]

[Abstract] A study is presented of the cardio- and hemodynamic effects of an aza-15-crown-5 derivative. Arterial pressure, pressure in the left ventricle, rate of contraction and relaxation of the myocardium, heart rate, blood volume per minute, venous return and perfusion pressure were recorded in 22 anesthetized cats. At 5-8 mg/kg, intravenous injection of the substance caused hypotension, dilation of arteries, negative iono- and chronotropic effects and decreased blood volume per minute. A possible mechanism of action of the substance is interference in calcium-ion metabolism. References 13: 5 Russian, 8 Western.

Influence of Dalargin on Microhemo- and Microlymph Circulation

18400496B Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104 No 3, Mar 88 (manuscript received 4 May 87) pp 300-302

[Article by V. K. Khugayeva, Laboratory of General Microcirculation Pathology, Scientific Research Institute of General Pathology andPathologic Physiology, USSR Academy of Medical Sciences, Moscow]

[Abstract] The mechanisms of action of dalargin have not been fully studied. This article studies the influence of dalargin on the microcirculation in blood and lymph microvessels. Experiments were performed on 30 male white rats anesthetized with nembutal. Microvessels 6-60μm in diameter and lymph vessels 40-200 μm in diameter were studied by flash lamp photography following application of dalargin to the surfaces of the vessels and IM in doses of 0.001 to 10 μg in 0.1 ml of 0.14 M NaCl, or 0.004-40 μg per kg body mass. Similar changes in microcirculation were observed by either method of application of dalargin. All doses studied increased the permeability of the vascular walls and activated lymph flow by increasing contraction of the microvessel walls. All doses caused identical levels of lymph flow from the mesentery tissue and activated contraction of the intestinal musculature. Figures 3, references 10: 9 Russian, 1 Western.

Peripheral Catecholaminergic Systems in Neuropeptide Antistress Effect

18400496C Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104 No 3, Mar 88 (manuscript received 17 Jun 87) pp 302-305

[Article by Ye. B. Khaysman, V. A. Arefolov and L. A. Malikova, Institute of Pharmacology, USSR Academy of Medical Sciences, Moscow]

[Abstract] A study is made of the effect of the opioid peptide dalargin and a new heptapeptide enkephalin analogue synthesized at the Institute of Molecular Genetics, USSR Academy of Sciences, by scientific research associates M.A. Ponomareva-Stepnaya and L.A. Andreyeva, under the direction of the head of the laboratory, candidate of chemical sciences V. N. Nezavibatko. Studies were performed on an immobilized stress model on 62 male rats. A histochemical fluorescent-microscopic method was used to reveal the adrenergic nerves. The preparations were injected intraperitoneally at 150 mg/kg and were found to have marked antistress effect, particularly dalargin. The observations indicate the possibility of effective adjustment of the mediator activity of the peripheral catecholaminergic systems under stress conditions using the neuropeptides studied. The greater antistress effect of dalargin is explained by the fact that its molecule has a terminal arginine component, giving the neuropeptide increased antistress action by stimulating the opiate receptors of the neuronal structures of the brain and by stimulating the inhibitory GABA-ergic system. The neuropeptides can therefore act as modulators of the functional activity of the sympathetic-adrenal system and of the adaptive properties of the organism in various stress stages. Figure 1, references 13: 11 Russian, 2 Western.

Content of Prostaglandins E_2 and F_2 in Dynamics of Development of Plague Toxin-Infectious Shock

18400496d Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104 No 3, Mar 88 (manuscript received 20 Jan 87) pp 313-315

[Article by T. D. Cherkasova, P. R. Vengrov, V. I. Melikov, V. P. Avrorov and V. A. Yurkiv, Laboratory of Infectious Disease Pathogenesis Molecular Bases, Central Scientific Research Institute of Epidemiology, USSR Ministry of Public Heath, Moscow]

[Abstract] A study is made of the content of prostaglandins in various organs and the blood plasma of rats during development of shock upon intoxication by mouse plague toxin, a complex lipopolysaccharide-protein system. Experiments were performed on Wistar rats following administration of 0.5 ml saline solution containing 0.5 mg (LD_{50}) of toxin into the caudal vein, or administration of the same solution inactivated by heating to 100°C for 20 minutes. Control animals received an equal volume of saline solution. The animals were sacrificed after 0.5, 2 and 5 hours, and the organs extracted and frozen in liquid nitrogen. Blood was taken from the heart in a chilled pipette containing 0.5 M EDTA one percent of the blood volume, pH 7.4. The results indicate restructuring of the cyclo-oxygenase path of prostagladin biosynthesis in all organs and the blood plasma. The initial preparation and the inactivated toxin had the same effect on the changes in prostaglandin concentration in all organs at all observation times. Activation of prostaglandin synthesis apparently results from the presence of a thermally stable lipopolysaccharide component, the plague bacterium endotoxin. The protein component of the mouse toxin apparently has no great influence on prostaglandin metabolism. References 15: 2 Russian, 14 Western.

Ultrastructure of Perilnfarct Zone Cardiomyocytes In Rats During Treatment of Experimental Myocardial Infarct With Hexapeptide Dalargin

18400496e Moscow BYULLETEN EKSPERIMENTALNOY BIOLOGII I MEDITSINY in Russian Vol 104 No 3, Mar 88 (manuscript received 10 Dec 86) pp 362-365

[Article by V. V. Khlystov, A. F. Usynin, V. S. Pavlenko and V. D. Slepushkin, Department of Pathology, Siberian Branch, All-Union Cardiologic Scientific Center, Academy of Medical Sciences, USSR, Tomsk]

[Abstract] A study is made to determine the most effective dalargin dose in experimental myocardial infarct, and to evaluate its influence on the periinfarct zone

cardiomyocytes at the ultrastructural level. Occlusion myocardial infarct was invoked in 76 white rats by ligature of the descending branch of the left coronary artery in the upper third. One hour after ligature, dalargin was administered intraperitoneally at 10, 50, 100, 500 and 1000 μg/kg. Twenty-four hours after occlusion the rats were decapitated, and the size of the left ventricular infarct zone was determined. Specimens were extracted from the periinfarct area and examined under an electron microscope. It was found that administration of dalargin soon after coronary artery occlusion had a protective effect on the periinfarct zone cardiomyocytes, causing most cells in this zone to retain viability, in doses of 50 and 100 μg/kg. Both higher and lower doses were less effective. Figures 2, references 15: 13 Russian, 2 Western.

GAPU Chief Discusses Pharmacy Situation

18400009 Moscow SOVETSKAYA ROSSIYA in Russian 17 Aug 88 p 3

[Interview with Aleksandr Dmitriyevich Apazov, chief, Main Pharmaceutical Administration of the USSR Ministry of Public Health (GAPU) by N. Fokina: "Where Do We Go for Medicine Today?"; no dateline]

[Text] [Question] "How long will this go on! The doctor prescribes a certain medicine and tells me right off that it can't be found in this city. But my baby is very sick, and I'm prepared to do anything—beg, grovel, write tearful letters to relatives: Help me find just a single wretched box of the medicine before I lose all hope. And am I really alone in this? Imagine how many people must stand in line at the pharmacy window, only to be courteously turned away...."

This letter written by T. Zakharova from Novosibirsk is but one in SOVETSKAYA ROSSIYA's mailbag. It is perhaps the most typical reflection of today's situation with drugs. Little Serezha, our reader's son, needs nootropyl. Imported drugs are one thing, but the letters are not concerned with them alone! Before this interview, Aleksandr Dmitriyevich, I also decided to stand in some pharmacy window lines to find out what people could get and what they couldn't get. I learned that things which would seem to be the most elementary are not to be had—cotton, valerian tablets, boric acid petroleum jelly, herb extracts....

Apazov: And what about mustard plasters? Did you ask about mustard plasters? Their absence is a real reflection of the level of our resources. The only plant that produces them—the Volgograd Mustard Plaster Plant of the RSFSR Gosagroprom—is perpetually behind by a third of its plan for supplying us. And this plan is only half of what we ask for—that is, only half of the actual health care needs. In the first half of the year, the pharmacy network is already undersupplied in mustard plasters by 466 million.

Let me show you an interesting newspaper clipping. Here is what the 8 December 1925 issue of PRAVDA said about the speech made to the First All-Union Congress of District Physicians by RSFSR First Peoples Commissar of Public Health A. N. Semashko: "Comrade Semashko dwelled on a large number of painful questions concerning medical services to the public. He pointed out the extremely bad situation with supplying our drug institutions with medicines. Their demand is being satisfied by only 74.4 percent...."

Fokina: Today, health care's is being provided with 70 percent of the drugs it needs. This figure was cited by USSR Minister of Health Ye. I. Chazov.

Apazov: Yes, the figure is about the same as it was 60 years ago. As you can see, the situation is a complex one, and the lack of medicines in the country is a highly neglected malady. In developed countries, drugs are the number one product, and they are given every priority. The world pharmaceutical industry is second in profits only to the military industrial complexes. But our approach is different. Although the sector's profitability indicator is not bad—over 10 percent—there is no possibility of rapid growth. Fixed capital depreciation is at 50 percent at medical enterprises—and at 100 percent at some. Moreover, this fixed capital is 96-98 percent utilized, while in Turkey, for example, it is 60-70 percent utilized, and 70 percent utilized in Yugoslavia. That is, those countries have a reserve which can be put into operation at any moment. We, on the other hand, are working on the edge.

Fokina: But it seems that the situation is changing. I know that around 4 billion rubles extra were allocated to a comprehensive program for development of the enterprises.

Apazov: But that is not the only problem. First of all, we need these drugs today, right now. And second.... Well, consider the difference between medical gypsum and ordinary gypsum. The former is much more expensive to produce—its purification and recovery are more complex. Of course the enterprise is not interested in producing it! And this is the way things are wherever medical products are the secondary and not the primary products. As an example, the Verkhnedneprovsk Starch and Molasses Combine of the UkSSR Gosagroprom, which supplies glucose to us, traditionally satisfies only half of our order. And just try to influence it with the powers of persuasion! What we need is an economic lever. But there is none.

So what does the USSR Gosplan go and do in this situation? It diverts drugs from the group of goods for public consumption. From my point of view, we shouldn't even compare medicines with consumer goods—the former are so much more important. But here we have the Leningrad Medical Polymers Plant, which has increased production of soap dishes and juice extractors, rather than systems for taking and transfusing blood, blood substitutes, and other injectable solutions, the production of which is labor-intensive. The situation with these devices is desperate. Last year, we asked for 100 million such disposable systems—and we were refused. We dropped the plan to 36 million. And in 1990 we would like to have 200 million, but they promise us almost four times less. And so it happens that, in all, medical products account for one-half of one percent of the total volume of our country's industrial production. By comparison, the figure is 2.8 percent in Hungary and almost 2.5 in Japan.

Were are we to go for medicine in order to compensate in at least some way for the shortfall? People should not be made to suffer! So we are forced to make purchases abroad. Today, only 59.3 percent of all drugs are produced domestically. We buy the rest. We buy 38.6

percent from socialist countries, mainly under the program for specializing production among CMEA countries. We buy around 2 percent from capitalist countries.

Fokina: Aleksandr Dmitriyevich, sad as this may sound, imported drugs are often preferred over Soviet-made drugs.

Apazov: What can I say, it is hard to argue with that statement today. We are in fact behind in quality of drugs. And if we compare the assortment produced by our industry even with the assortment of socialist countries, we see how limited our health care is in its selection of drugs. Many medicines are simply unavailable to us! There are no highly effective cardiovascular drugs, the latest antibiotics (so-called "reserve antibiotics") are unavailable, there are no aerosols for treatment of bronchial asthma, and there are practically no hormonal drugs or protein supplements for postoperative patients. And alas, our doctors would be unable to transplant organs, were it not for the drugs supplied by the West. And that's not all. Even when we consider such purchases, our health care workers have a great deal fewer opportunities than do their foreign colleagues. Take even Poland, for example. It sells us reasonably good drugs, but when it comes to its own needs, it purchases the latest drugs from capitalist companies. Our resources for doing so have always been extremely limited, and now allocations for purchasing drugs in capitalist countries are even decreasing. We are purchasing enzymes (festal, pancreatin, panzinorm), psychotropic drugs and gastrointestinal drugs in smaller quantities. I cannot understand why we buy blouses from India which possibly provide some esthetic satisfaction to some people, when human health is so much more important. Can it possibly be that Yugoslavian dishrags for washing plates and glassware are more vital than drugs to treat Parkinson's disease, which have been so difficult to get in our country?

Fokina: But we cannot always count on help from our foreign partners, on what they can produce there and what we can purchase from them. In my opinion, we're on the right road when we invest money into the development of our own medical industry. We have already dropped 18 imported medicines from our purchases because we can produce them ourselves.

Apazov: I would add another 34 to the figure you just cited. We have reduced purchases of these drugs by increasing our own production. Before the five-year plan ends, industry must assimilate production of over 100 new drugs and medical items. Among them are immunomodulators, biostimulants and drugs stimulating and restoring excitability of nerve and muscle tissue. I agree with you absolutely: We cannot be totally dependent on imports.

We know what human pain is, we see the tears of those who have lost hope and faith that they can get relief from their torment. We see what neither the institutes that develop drugs nor the plants that produce them can see. Yes, the pharmacy worker receives the entire brunt of the unquestionably valid indignation. But since we don't produce the drugs, what can we do?

First of all, progress is already being made in our relations with the medical industry. We meet more often, we understand one another better, and we understand the most important thing: We are working for the same goal, and we share a common concern—the health of the Soviet citizen. We have managed to lessen the dictatorial manner from which we have suffered for many long years. The way things were then, we had to take what they gave, and be thankful for that. But now we want to turn things around so that we determine the quotas for industry, and not vice versa. But this is a difficult process, and we don't always achieve positive results. We can now make adjustments in our orders (before, they were written up a year in advance—just try to predict outbreaks, epidemics and so on in those circumstances). We are reviewing the assortment of medicines produced by our industry. Six hundred ineffective and obsolete drugs have already been discarded. Proposals to discard another 222 drugs from the State Register have been sent to the Pharmacological Committee.

But there is a subtle force at work here as well. It takes generations for the demand for many drugs to die out. For example, senior citizens still ask for Karmanov's tablets in the pharmacies. They have gotten used to them, and it seems as if nothing else helps. The same can be said for fish oil, which was replaced by vitamin D and videikhol long ago. But obsolete drugs must be removed from production. Their place will be taken by much more effective drugs. For example we are now receiving many more cardiovascular drugs, antiseptics and analgesics. This represents a fundamental change, since it is improving the quality of medicinal care. We have even gone so far as to draw up a list of the most important drugs—around half a thousand names. And we have set the Ministry of Medical and Microbiological Industry the priority task of increasing its production to the levels needed by health care.

Fokina: Incidentally, the quotas for drug purchases have now been increased for hospitals and polyclinics. We seem to be experiencing a unique boom in the use of drugs owing to this as well. How are the pharmacies reacting to this increase? Could they relieve the stress at least a little by reorganizing their work?

Apazov: Of course. In former times, pharmacies were not economically interested in considering the interests of the patient. Absurd as this may seem, planning organs treated pharmacies as trade organizations and determined their plans on the basis of gross sales. Such plans could be fulfilled by selling not only medicines but also, for example, an imported toothpaste in short supply. And even today the pharmaceutical service is listed under the "retail trade" subdivision of the classification system used by the USSR Gosplan and the USSR State

Committee for Statistics. This is something we need to dismantle. The spirit of trade is not only alien but also harmful to pharmacies. They are supposed to be dispensers of mercy! Out of sympathy for the individual who has turned to them for assistance. New indicators will be introduced into the work of the pharmacies beginning in November. Their purpose is to provide every Soviet citizen all of the medicine he needs, promptly. We feel that this should be the end result of the work of the pharmacist.

The second indicator of a pharmacy's work is profit. It is something that is necessary if the pharmaceutical service is to develop. And if we are to stimulate the worker to fulfill the first, qualitative indicator. That is, we are economically strengthening the lowest link by endowing it with independence, rights, and, of course, responsibility.

Fokina: Excuse me, Aleksandr Dmitriyevich, but isn't this the way things are supposed to be anyway?

Apazov: Yes, it is. But consider how many obsolete rules we still have to follow! For example, there is a particular shipment norm for every drug. If we order less than the norm, industry will not accept the order. And if the annual demand of some region is equal to this norm, it will receive a shipment just once a year.

There is one other rule that I believe to be obsolete: Not by any stretch of the imagination can all wholesale bases receive pharmaceutical freight. And yet they are the main supply links, responsible for prompt delivery of medicines to the public. If we say that medicine has been living on the leftovers of the economy, then we would also have to say that the warehouse system of the pharmaceutical service has been living on the leftovers of medicine. Each day 150-200 containers of drugs being sought by people throughout all of Moscow accumulate at the approaches to Moscow.

Fokina: There are 30,000 pharmacies in the country. Sometimes it happens that products that accumulate in one place are unavailable in another. Were the pharmaceutical service to possess an automated control system, complete information would be available on drugs.

Apazov: We have already drawn up the program. We have also purchased and are now installing some of the equipment. At the Union level for the moment, of course. But next year, we will begin introducing the automated control system into the republics. The process is being held back by the absence of microprocessor equipment.

Fokina: On the other hand, isn't it a little silly to dream about computers when the pharmacies don't even have respectable scales?

Apazov: Unfortunately, that is the way things are in some places. But it is also a fact that hundreds of thousands of pharmaceutical workers must perform manual labor, which is not very productive. The wages for this labor run in the hundreds of millions of rubles. Each year the pharmacies produce over 3.5 billion units of packaged goods. This is the source of our poverty: All labor expenditures are treated as expenses of the pharmaceutical service. The cost of a drug includes only that of the drug itself and the container. A hospital, for example, can buy one bottle of industrially produced intravenous solution for 1 ruble 23 kopecks, but it can buy the same from us for 25 kopecks. The cost of manufacturing this product in a pharmacy is 60 rubles! From that, the losses of the pharmacies total 400 million rubles each year.

Fokina: I hope, Aleksandr Dmitriyevich, that you are not suggesting solving the problem by raising prices?

Apazov: That would be the last way in which I would want myself to be interpreted. Drug prices have been reduced four times since 1982. I believe this to be the absolutely correct line. But it is our bad luck that almost half of the drugs and medicines are unprofitable to the pharmaceutical network. Of 1,637 Soviet-made drugs, 267 are unprofitable, and the retail prices on 96 types of herbs are much lower than the wholesale prices. This situation must be changed. But how? In my opinion, we need to establish a new procedure for settling accounts with enterprises. Drugs should be sold at retail prices, with a single rebate that would ensure the needed profitability level for the pharmacies. And of course, we need to introduce wages for the preparation of medicines in the pharmacy. Moreover these expenditures must be absorbed by the state, and not the pharmaceutical service.

Allocations for both the maintenance of existing treatment and prevention institutions and the construction of new ones have increased significantly. But the effectiveness of treatment depends not only on the material base of health care, but also on unconditional supply of all of the drugs the treatment process needs. Even if health care were to make great advances, while the pharmaceutical service remained the same, people would not feel the results of reform. In order for this not to happen, we need to give priority to drugs, both in production and in purchases abroad.

Fokina: We have returned to the starting point of our discussion, Aleksandr Dmitriyevich. Let us answer the main question troubling our readers: Where are they to go for medicine today?

Apazov: To the pharmacy. I think that many have already noticed that progressive forms of service have been introduced. We are now taking drug orders from physicians by telephone, we make home deliveries, and we send postcards to people as soon as the drugs they need come in.

It is our goal to help the individual. Not a single person should lose hope at the pharmacy window. His health and the health of the Soviet people represent the purpose and sole reward for which we work today.

From the Editor

A number of fundamental issues were posed in the interview with A. D. Apazov, chief of the Main Pharmaceutical Administration of the USSR Ministry of Health. Full satisfaction of the population's drug needs by 1993—a goal posed in government decrees—depends on resolution of these issues. The issues are within the competency of the USSR Gosplan, the Ministry of Medical and Microbiological Industry, the Ministry of Chemical Industry, the Ministry of Petroleum Refining and Petrochemical Industry, the Ministry of Timber, Pulp and Paper, and Wood Processing Industry, the Ministry of Instrument Making, Automation Equipment and Control Systems and the USSR Gosagroprom. The editor's office of SOVETSKAYA ROSSIYA hopes to receive exhaustive answers to the questions posed in this article from the executives of these organizations, including ministers V. A. Bykov, N. V. Lemayev, Yu. A. Bespalov, M. I. Busygin and M. S. Shkabardnya.

Excessive Pesticide Use in Azerbaijan Causes Health Problems

18400043 Moscow TRUD in Russian 25 Aug 88 p 2

[Article by T. Kasumov, Minister of Health of the AzSSR: "Poisoned Earth: The Consequences of Excessive Use of Pesticides on the Fields of Azerbaijan"]

[Text] Our torrid steppes—Mil, Mugan, Shirvan—extend over many hundred hectares. If there were water here, long ago orchids would have flowered, plowed fields would have grown. But it is considered that this land is best suited for growing cotton. And so, no matter which direction you take across Mil or Mugan, on both sides of the road, as far as you can see, to the horizon itself are cotton fields.

This crop occupied a firm place in the republic's agriculture. Indeed, it is the priceless treasure of our land. But, because we did not know how to use it properly, having turned this blessing into a curse, today we are paying the price.

"Let the cotton grow up to meet the clouds.." How could the poet have imagined, when he composed this high-flown metaphor, that it would be taken completely seriously, with no regard for the actual capacity of the land, and become the battle cry of the times of stagnation? That it would become an end, to attain which all means were justified.

In the drive for instantaneous results, in the endeavor to attain the greatest possible harvests, everything was permitted—exhausting 12- to 13-hour days for the rural population (everyone, without exception, pregnant women, children, and even medical personnel, who were compelled to leave their patients to their fates), and expanding the areas under cultivation until they came right up to the peasants' yards and gardens, and finally massive multiple chemical treatments, primarily from aircraft, so that pesticides lay in a thick film not only on the fields, but on meadows, pastures, and waters. Sometimes it happened that they sprayed poisonous chemicals literally on the heads of people who had not managed to take cover from the unexpected—unscheduled and unannounced—flights of the aircraft. And more often than not this was a preparation of DDT, this same highly toxic pesticide the use of which in agricultural production was officially prohibited in 1970. As a rule, every year the republic's Council of Ministers petitioned the USSR Ministry of Health, and without any special objections, the chief public health physician of the country gave permission for the use of DDT in the agriculture of Azerbaijan "as an exception."

How many of them there were, these exceptions!

Azerbaijan has the highest per hectare use of pesticides in our country.If this parameter fluctuates between 2 and 5 kilograms for the Soviet Union as a whole , then in our cotton growing and vegetable growing areas this parameter reaches 40, while in vineyard areas it goes as high as 183 kg. At the same time, according to data from the World Health Organization, the mean use of pesticides was 1.9 kg per hectare in European countries, 1.5 kg in the U.S., and 0.13 kg in Latin America.

Relatively little subject to biodegradation, DDT and other dangerous pesticide will be retained for a long time in the cycles of nature, with all the attendant consequences. Moreover, we are already feeling these consequences now. The trees dying at the roots, the foliage falling in the middle of summer, the poisoned rivers and lakes, the earth so full of poisons that now and for long to come it will not be able to bring forth healthy fruit. This, alas, is the sad reality of the majority of our cotton-growing regions. An analysis performed by scientists of the republic SES (Sanitary Epidemiological Station) has shown that the maximum acceptable concentration of pesticides is exceeded by many times in every fourth food product sample tested from the Neftechalinskiy rayon, in every eighth sample from the Bardinskiy rayon, and in every tenth sample from the Zhdanovskiy rayon.

All these gross violations cannot help but have their effects on the health of the populace.

A multifactor comparative study performed in two farms in the Agdashskiy rayon disclosed a very striking pattern. The parameters of overall susceptibility to disease in children 6 years old and younger in the area most polluted with chemicals (the Uzbekistan kolkhoz) was 4.6 times higher, than in an area with minimal chemical pollution (the Kavkaz kolkhoz). Included in this figure was an increase of skin disease by a factor of 5.6 and an

increase in chronic nutritional and metabolic disease by a factor of 4.2. Diseases of the nervous system and respiratory tract were elevated by a factor of 3.1, while general reactivity decreased by a factor of 2.5, and growth and physical development was retarded by 12 percent in children less than a year old. Moreover, one of the major causes of high child mortality rate in rural regions is also pesticides. These are striking, scandalous facts. Here is the high price we have paid—the price of the health of the population, of our future generations—for our "resounding" victories during the time of stagnation, victories which have led to our current defeats.

At present, things are beginning to improve somewhat. During the past year, the assortment of highly toxic pesticides in use has decreased, and natural means of protecting plants have come into more extensive use. Public health monitoring of the use of poisonous chemicals has become stricter and measures have been taken to improve the preventive medical examination of rural workers. And yet it cannot really be said that these shifts have already begun to have a significant effect on the state of affairs.

How can we explain the fact that the use of pesticides has remained unjustifiably high, while at the same time scores of tons of microbiological preparations for use against pests must be destroyed since they have not been used in time and have lost their efficacy? Why in 70 percent of the cotton farms studied in a number of regions are chemical poisons kept in sheds, in unadapted storehouses and even out in the open, to be scattered by the winds and washed off by the rain? Why, to this day have they not yet resolved the issue of destruction and burial of no longer usable or prohibited pesticides, which are now accumulating on the farms in enormous quantities, while the opening of the republic's only waste disposal site suitable for such purposes is postponed from year to year?

Frequent relapses of an old disease are particularly disturbing. In March of last year, the chief public health physician of the USSR prohibited the production and use of butifos, a highly toxic pesticide, extremely dangerous to public health and the environment. And a half year later, our public health service discovered that in certain rayons, especially in Salyanski and Neftechalinskiy, this chemical was in extensive use for the defoliation of the cotton plants. It transpired that the permission for this was given by the chairman of the All-Union Association of "Soyuzselkhozkhimiya" [Union of Agricultural Chemistry], A. Gulenko, the same individual who so blatantly violated the prohibition of the State Public Health Commission organs. How are we to evaluate such atrocities from the standpoint of today? And is there a guarantee that such things will not happen in the future?

Conjointly with the trade unions, we have taken measures to ensure that in the future the situation will be monitored unflaggingly. But we must frankly acknowledge that it is difficult to count on success without changes in the attitudes of the farmers, the rural workers themselves. Obviously, in addition to the use of stricter measures to punish violators, we also need broader based, explanatory propaganda. The years of silence, of creating the illusion that all was well in all areas, including the ecological, have taken their toll. We still cannot decide to provide completely open information on the true state of affairs. It has become urgently necessary to speak out at the top of our lungs about the true situation, to regularly publish reports on the concentrations of harmful substances in the air, soil, and in the agricultural products which are frequently sold in the marketplace without any monitoring or control.

Of course, all this will entail no few problems. The technical facilities and equipment of our laboratories are extremely weak; there is an acute shortage of workforces trained in the appropriate technologies. The monitoring and analytic department of the State Agricultural Industry has turned out to be unable to provide the requisite amount of research even now. And yet the problem has to be solved.

In this area, we are placing great hopes on the long-term comprehensive program, "Health of the population of the Azerbaijan SSR," currently being developed in response to an initiative of the new leadership of our republic. Thrown open for discussion by the public, it will have the capacity to involve all strata of the population in developing concrete measures to improve public health, protect the environment, and provide for rational use of national resources. These are the people who will continue to live and work on this earth, saving and conserving it for future generations.

Child Mortality, Lack of Resources in Central Asia

18400042 Moscow IZVESTIYA in Russian
11 Sep 88 p 1

[Article by S. Tutorskaya: "What Medical Statistics Tell Us: The Status of Child Health in Our Country Remains Disturbing"]

[Text] As the first deputy minister of health of the USSR, I. Denisov, said recently, last year 264 out of every 10 thousand newborn infants died. This is the average; but if you look at the statistics region by region, you will find that in the republics of Central Asia and in Kazakhstan the infant mortality rate is higher—446 deaths, compared with 167 in the European portion of the country. The highest infant mortality rate—nearly 60 deaths for every thousand births—is in Checherno-Ingushetiya. These figures were announced at the meeting of the board of the USSR Ministry of Health, where scientific-clinical regional programs to preserve the health of mothers and children were ratified.

Nowhere will the long silence, the absence of glasnost be as difficult to make up for as in this area of public health. For many years statistics on child mortality were kept

secret. It now turns out that the hourly, inexhaustible concern about mothers and children existed more on paper than in reality. Until very recently, the resources and efforts directed at this extremely important area were immeasurably lower than the actual requirements. And to make matters worse, the measures taken were based on "averaged" plans, which did not take account of actual conditions. For example, in the republics of Central Asia, in contrast to the Baltic republics, children constitute quite a high percentage of the population. However, physicians were sent to and trained for these "child-heavy" regions, without any consideration of this important circumstance. The result was a very acute deficit in the numbers of pediatricians and obstetrician-gynecologists in the republics of Central Asia and Azerbaijan.

At the behest of the USSR Ministry of Health, a group of scientists and physicians studied the status of this problem in the Lithuanian SSR and Turkmeniya. They found, for example, that a Turkmen obstetrician was tremendously overworked, handling three times the number of births ofhis Lithuanian counterpart. What can be said about the quality of maternity services when the physician who holds in his hands the lives of mother and child frequently works around the clock?

Beginning with the characteristics of the family organization, the traditions associated with birth rate and ending with the causes of child illness and mortality during the first year of life, the two republics are very different. Thus it follows that work in family planning, preventive medicine, and social services must also be conducted differently.

Alcoholism in mothers does enormous harm to the health of the baby. But if this problem exists in Lithuania, it is virtually nonexistent in Turkmenia. On the other hand, if we are talking about the traditions of maternal nutrition, dictated by age-old ways of life, then, on the contrary, greater public health and educational work is needed among Turkmen mothers. Many of them suffer from anemia and vitamin deficiencies.

It is also essential that we build modern hospitals for children. There are whole regions where not a single one has been built for a decade. In Volgograd there is no children's hospital for infectious diseases. Five small children (instead of one) are put together in an isolation room. And yet despite these circumstance, money allotted to building hospitals, was used to equip an eye clinic, ignoring the recommendation of the oblast health department. An eye clinic is of course necessary. But how could the RSFSR Ministry of Health take money away from the children for it.

Experience in other countries demonstrates that it is possible to decrease child mortality significantly in a short period of time, and improve the health of mothers and children, but this is not merely a matter of physicians alone. Concern for healthy working environments for women, establishment of prenatal centers where the state of the infants is monitored long before birth, genetic counseling, new benefits for pregnant women, nursing mothers and those with many children, free food and vitamins for children—these and many other measures have been stipulated in the regional programs. But they can be implemented only if the reserves of the whole society are mobilized. Without equipping the medical facilities with the most advanced medical technology (currently, they frequently cannot stand up to any kind of critical examination) and the necessary material expenditures, all these recommendations will remain merely good intentions.

UDC 616.379-008.64-08

Problems With the Quality of Treatment Given to Diabetes Mellitus Patients

18400426 Riga IZVESTIYA AKADEMII NAUK LATVIYSKOY SSR in Russian No 4, Apr 88 pp 98-101

[Article by Ye. V. Khanina, Riga Medical Institute]

[Text] Matters involving the quality of dispensary care given to diabetes mellitus patients have received little attention up to now.

The most important criteria for measuring the quality of treatment for diabetes mellitus are the indices for the level of metabolic control, the time of onset of late complications and how they are expressed, the frequency of acute decompensation incidents, indices of temporary and long-term disability, and the frequency of hospitalization. At present, the need for collaboration between physician and patient is a must if long-term control of diabetes is to be achieved, and the patient must be armed with specific knowledge and practices.

In the opinion of a number of researchers,[1-3] the level of control of diabetes depends on how much the patient knows about his own illness and the psychological state accompanying it.[4]

In light of the extremely scant information on the nature of diabetes mellitus control[5,6] and the absence of work involving level of knowledge and the effect of psychological state on the nature of control, we decided to study such matters. We developed special questionnaires for that: the "Evaluation of the Level of Knowledge and the Nature of Compensation" and the "Psychological Questionnaire for the Diabetes Mellitus Patient."

The first took into consideration the stage of diabetes, complications, and accompanying diseases. The patient answered questions on the feasibility of diet planning, on whether or not he knows the symptoms of acute diabetic decompensation and the complications that attend the long-term course of diabetes, and on whether or not a test for glucosuria or for acetone in the urine is performed at home. Disability, frequency of hospitalization, average glycemia levels for a year, the presence of

ketonuria, and lipid metabolism indices were taken into account. The psychological questionnaire ascertained the patient's relationship to the diabetes, whether or not he would be apt to follow the physician's recommendations strictly, and the patient's dietary habits. It ascertained what problems the patient had in connection with the diabetes (such as family problems and occupational problems) and who would help to resolve them. The patients were designated optimists or pessimists, depending on their responses.

The results of the investigation were processed by computer with a program we developed specially for use with BMDPI, a package of programs from California for processing medical information.

In outpatient practice, diabetes control is assessed on the basis of glycemia level, which is usually determined in a single test, on an empty stomach, once a month. For control characteristics, we computed glycemia levels averaged over a year's time or longer before the research, which involved no less than 10 analyses. The control levels were assessed in the following manner:

For Diabetic Patients

Type I	Type II
5.5-8.3 mmole/l, good control	lower than 6.5 mmole/l, good control
8.4-11.1 mmole/l, satisfactory control	6.6-8.5 mmole/l, satisfactory control
11.1 mmole/l, unsatisfactory control	above 8.5 mmole/l, unsatisfactory control

In all, we examined 270 diabetes mellitus patients—121 men, 149 women—of whom 160 were type I and 110 were type II.

The causes for acute diabetic ketoacidosis and diabetic coma were analyzed separately in 30 diabetes mellitus patients.

Below we cite, in percentages, the level of diabetes control in the patients we studied: 5.5 percent of type I patients had good control, 12.7 percent had satisfactory control, and 81.8 percent had unsatisfactory control; good control was noted in 19.5 percent of the type II patients, satisfactory control in 15.8 percent, and unsatisfactory control in 64.7 percent.

Thus, the level of control in diabetic patients is extremely low, especially with type I diabetes mellitus.

After analyzing what those we studied knew about diabetes, we must say that they know very little. Some 20.4 percent of type I patients, for example, did not know the symptoms of hypoglycemia. Some 70.7 percent of type I patients and 98.2 percent type II patients were unfamiliar with the symptoms of ketoacidosis. None of those we surveyed monitored themselves at home for glucosuria or determined the acetone in the urine. Only seven type I patients and two type II patients could answer the question about calories [kalorazh]; not one patient we surveyed had engaged in dietary planning.

The analysis we did to correlate nature of diabetes control with level of knowledge about diabetes and psychological attitude of the patient was unable to identify a substantial relationship, perhaps because of the extremely low percentage of individuals with good knowledge of diabetes and good diabetes control.

We were also unable to identify correlations between level of knowledge and stage of diabetes ($r = -0.08$), age ($r = 0.064$), sex ($r = 0.05$), or social status ($r = 0.08$).

The table cites the frequency principal complications of diabetes mellitus and accompanying diseases in percentages among those we studied.

Frequency of Diabetic Complications and Principal Accompanying Diseases in Types I and II Diabetes Mellitus, in Percentages

Complications and Accompanying Diseases	Type I	Type II
Retinopathy	55.5	59.4
Polyneuropathy	51.8	53.0
Posthypoglycemic encephalopathy	6.6	—
Macroangiopathy of lower extremities	16.1	40.6
Obesity	14.4	67.2
Hepatosis	14.6	36.5
Vulvitis	3.6	5.3
Ischemic heart disease	7.2	30.1
Arterial hypertension	7.7	21.2
Pyelonephritis	3.3	6.2
Pancreatitis	6.1	5.3
Cholecystitis	1.1	4.2

Thus, the frequency of diabetic retinopathy and polyneuropathy among types I and II diabetes in the patients we studied was not appreciably different (p greater than 0.05), whereas accompanying diseases such as macroangiopathy of the lower extremities, obesity, hepatosis, ischemic heart disease, and arterial hypertension are noted considerably more often in type II diabetes mellitus (p less than 0.05).

We analyzed the causes of the onset of ketoacidosis in 30 diabetes mellitus patients who entered the Seventh Riga City Clinical Hospital in a state of diabetic coma or precoma. Below is a distribution of the causes in percentages:

Unwarranted reduction in insulin dose	16
Unwarranted postponement of insulin	16
Intercurrent [interkurentnyye] diseases	24
Dietary Excesses	12
First-time diagnosis of diabetes mellitus	12
Consumption of alcohol	4
Undetermined cause	16

Thus, improper behavior on the part of the patient was the cause of diabetic decompensation in most cases.

The extremely low level of diabetes control that we identified, the low level of knowledge about the disease in the majority of the diabetics we examined, and the high percentage of complications point to the need to improve the treatment of diabetes patients in the outpatient system. We feel that one way of doing this would be to set up a center for teaching patients a system of self-management that would include specific practices involving, for example, dietary management, self-control of blood glucose levels, and prevention of complications. This knowledge and practice is necessary if one is to have the proper relationship to the treatment of diabetes and achieve the best control of the disease.

For an objective assessment of the level of control of diabetes, glycosylated hemoglobin determination, which is now acknowledged as an integral indicator of the homeostasis of glucose for a period of up to 80 days preceding the examination,[7,8] must be introduced on a broad basis in the outpatient system.

We have set up offices for educating diabetics in the Seventh Polyclinic and the Seventh Clinical Hospital. The training is done with an 8-lesson program we developed. Over the length of the course, the patients get specific information and learn specific practices, which leads to better control of diabetes.

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UDC 616-006.04-036.22-07(477)

Improved Prediction of Cancer Incidence in Ukraine for 1990

18400037a Leningrad VOPROSY ONKOLOGII in Russian Vol 34 No 4, Apr 88 (manuscript received 23 Jul 85) pp 405-410

[Article by L. N. Guslitser and Ya. D. Matviychuk, Institute of Oncologic Problems imeni R. Ye. Kavetskiy, Ukrainian SSR Academy of Sciences, Kiev]

[Abstract] A 16-year time period was analyzed for the morbidity patterns of neoplastic conditions in Ukraine in order to obtain an accurate prediction of cancer incidence in Ukraine for 1990. The study involved a careful assessment of data on age factors of male and female cancer incidence for the periods 1965-1972 and for 1965-1980 in order to arrive at predictive data for 07/01/99 with p = 95 percent. Extrapolation of malignancy incidence in terms of age and sex showed that by 07/01/99 the overall cancer incidence for both men and women will continue to increase, with a further increase in the incidence of oral, pharyngeal, rectal, respiratory, hemopoietic, and lymphatic malignancies. In addition, the data also indicated an increase in the incidence of laryngeal cancer in men and of breast cancer in women. However, the data were also consonant with an expected reduction in the incidence of lip, gastric and esophageal cancers by 1990 in the Ukraine, as well as in cervical cancer in women. In part, the anticipated increase in the overall cancer incidence in the Ukraine is related to the aging of the population. References 18: 14 Russian, 4 Western.

UDC 616-006.04-07:614.1

Improvements in Soviet Cancer Registry

184000037b Leningrad VOPROSY ONKOLOGII in Russian Vol 34 No 4, Apr 88 (manuscript received 24 Nov 86) pp 410-416

[Article by V. V. Dvoyrin, A. Ye. Okeanov, and R. B. Suveyzde, All-Union Oncological Scientific Center, USSR Academy of Medical Sciences, Moscow; Scientific Research Institute of Oncology and Medical Radiology, Belorussian SSR Ministry of Health, Minsk; Latvian SSR Oncological Dispensary, Latvian SSR Ministry of Health, Riga]

[Abstract] Recent surveys have shown that the Soviet cancer registry is in considerable need of revision and implementation of new policies and practices to improve

its authority as a data base. Analysis of data for 1985 revealed disparities between the various republic th at ranged from 20- to 70-fold for the various forms of malignancies, age, and sex factors. However, a closer look revealed that rather than representing factual medical statistics, the data were unduly biased by local practices in record keeping, data evaluation, and clinical interpretations. To insure greater uniformity and reliability of the cancer registry information more simplified record-keeping practices have been introduced. For example, the patients are to be classified on the following four treatment categories: 1) surgical only, 2) surgery + radiotherapy, surgery + chemotherapy, surgery + chemotherapy + radiotherapy, 3) single-modality radiotherapy, and 4) combination radiotherapy. The designation "chemotherapy" has been modified to include drug, hormone, and immunotherapy and their combinations. Consequently, all patients that had undergone cancer treatment should fall into one of these four categories. With additional simplifications the entire system may be expected to provide a more reliable and accurate measure of cancer in the USSR. Figures 1; references 2 (Russian).

UDC 336.121.36:061.62

Role of Self-Financing in Budgeting for Medical Scientific Production Associations

18400489a Minsk ZDRAVOOKHRANENIYE BELORUSSII in Russian No 4, Apr 88 (manuscript received 18 Nov 87) pp 34-36

[Article by P. G. Rytik and A. G. Zhuravlev, Belorussian Scientific-Research Institute of Epidemiology and Microbiology]

[Abstract] Two recent developments aimed at improving the operations of scientific-research organizations are the decree of the Central Committee of the CPSU and the Council of Ministers of the USSR on "Conversion of Scientific Organizations to Full Economic Accountability and Self-financing" and the USSR law on State Enterprises. The Belorussian Scientific Research Institute of Epidemiology and Microbiology is examined as an example of the evolution of the concepts associated with the principles for financing research institutions. From 1924, when it was first organized, to 1965, the institute functioned as a single entity financed by a single budget, permitting economy of resources, creating a healthy interaction between scientific and production personnel, and facilitating an expedient flow of operations from the bench to production. In 1965 the research and production operations were separated for financing and operati[illegible]poses. This led to considerable duplication of re[illegible]s and personnel and resulted in a drop in productivity. The third period began with the above noted legislation, which reinitiates the close relationship between the scientific and the production facilities. This is viewed as a considerable improvement and should turn the institute into a profit-making entity.

Regional Specifics of Cancer Control Education

18400515a Leningrad VOPROSY ONKOLOGII in Russian Vol 34 No 5, May 88 (manuscript received 8 Apr 87) pp 593-600

[Article by A. V. Chaklin, I. L. Miliyevskaya and M. V. Maksimova, All-Union Oncologic Scientific Center, USSR Academy of Medical Sciences; Central Scientific Research Institute of Sanitary Education, USSR Ministry of Public Health, Moscow]

[Abstract] Cancer control education must be oriented toward individual groups of the population. A survey of 3,442 persons in Moscow and the republics of Central Asia and the Northern Caucasus, indicated some improvement in cancer knowledge, but a need for continued education. Large groups of the population are found to intentionally avoid cancer screenings, and most persons are unwilling to receive cancer-prevention treatment. Less than half the population believes that a healthy lifestyle can aid in prevention of cancer. Important areas requiring emphasis in cancer education include encouragement of the population to have regular physical examinations and adopt a more healthy lifestyle, including avoiding smoking and excessive drinking. References 10: 5 Russian, 5 Western.

Organizing Republic Endoscopic and Cytologic Centers For Active Screening For Precancerous and Cancerous Diseases of the Cervical Canal and Corpus Uteri

18400515b Leningrad VOPROSY ONKOLOGII in Russian Vol 34, No 5, May 88 (manuscript received 27 Jul 87) pp 605-608

[Article by L. N. Mkrtchyan, A. M. Ambartsumyan, G. A. Arzumanyan, A. G. Madoyan and Zh. S. Shakhnazaryan, Oncologic Scientific Center imeni V. A. Fanardzhyan, Armenian Ministry of Health, Yerevan]

[Abstract] A system of active screening for precancerous and cancerous disease of the cervical canal and corpus uteri has been introduced at the Republic Endoscopic Center and the Republic Cytologic Center, both associated with the Armenian Ministry of Public Health. A comparative analysis of five methods was performed, based on examination of 504 women from a risk group. Aspiration by means of plastic catheters was found to be almost as informative as histerobiopsy, while being much more suitable for mass screening, requiring no special instruments, and being completely atraumatic because of the flexibility and elasticity of the catheter. Cytologic examination of materials obtained by plastic catheter was found to be quite effective for detection of glandular hyperplasia and cancer. Morphologic examination of biopsy material from 28 women with polyps and 52 with endometrial and cervical canal hyperplasia revealed precancerous phenomena in 20 percent and cancer of the endometrium or cervical canal in 5.2 percent of this high oncologic risk group. References 5: Russian.

UDC 615.849.2:546.799.4.02.239].015.4

Biological Activity of Inhaled ^{239}Pu Coupled With Experimenta: Treatment With Zn- or Cu-DTPA Complexes

18400501a Moscow MEDITSINSKAYA RADIOLOGIYA in Russian Vol 33 No 5, May 88 (manuscript received 23 Feb 87) pp 58-61

[Article by Ye. G. Sinyakov, A. P. Nifatov, E. R. Lyubchanskiy, and A. G. Bazhin]

[Abstract] The modifying effect of Zn- and Ca-DTPA on the biological activity of high doses of inhaled ^{239}Pu was studied on Wistar rats. After initial inhalation of Pu-nitrate, various study groups were treated for up to 8 weeks with Zn- and Ca-DTPA (therapeutic dose: 0.5 ml, 25 micromole/kg intraperitoneally, daily). Overall, the levels of observed Pu were decreased 2-fold in the lungs, 3-fold in skeleton, and 4-fold n the liver. The mean lifespan of the contaminated animals was extended, and the frequency of development of pneumosclerosis was reduced. Animals developed tumors at various sites, predominantly in the lungs. Zn- or Ca-DTPA therapy is recommended after inhalation of substantial amounts of ^{239}Pu. References 6: 5 Russian, 1 Western.

UDC 576.809

Polypeptide E Surface Antigen of Tick-Borne Encephalitis Virus (TBEV): Functional Role of Tertiary Structure

18400016a Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 301 No 3, Jul 88 (manuscript received 28 Jan 88) pp 728-730

[Article by M. F. Vorovich, A. V. Timofeyev, D. G. Maldov, and L. B. Elbert, Institute of Poliomyelitis and Viral Encephalitides, USSR Academy of Medical Sciences, Moscow]

[Abstract] An analysis was conducted on the functional role of the tertiary structure of polypeptide E, a surface antigen of TBEV, in terms of infectivity, antigenicity, and hemagglutination. Tertiary structure was altered by treatment with reagents disrupting S-S bonds (dithiothreitol, dithioerythreitol, or beta-mercaptoethanol), followed by appropriate testing of the parameter of interest. Disruption of the disulfide bonds was found to alter each of the functions under discussion. The loss of infectivity and hemagglutinating activity was attributed to alterations in functional groups responsible for binding to cellular receptors. In addition, immunoenzyme assays demonstrated that antibodies elicited against the native virus reacted poorly with TBEV on which the tertiary structure of polypeptide E had been chemically modified, indicating that such viruses are unsuitable for the preparation of vaccines. These observations demonstrate that a key factor in developing genetically engineered TBEV vaccines must include retention of the native conformation of polypeptide E. Figures 1; references 11: 4 Russian, 7 Western.

Conference on Microbiological Synthesis Apparatus Held in Yurmala

18400322 Riga IZVESTIYA AKADEMII NAUK LATVIYSKOY SSR in Russian No 2, Feb 88 pp 126-127

[Report on conference by M. Kristapsons: "Bioengineering-87"]

[Text] The All-Union conference "Modern Tendencies in the Development of Apparatus for Conducting Microbiological Synthesis Processes" ("Bioengineering-87") was held at the House of Science in Yurmala from 10 through 12 March 1987. Leading specialists of the USSR Academy of Sciences, the Ministry of Higher and Secondary Specialized Education, the Ministry of Chemical and Petroleum Machine Building, and the Ministry of the Medical and Biological Industry working in the field of bioreactor building were invited to the conference organized by the Scientific Council for the Overall "Microbiology" Problem of the USSR Academy of Sciences and by the Institute of Microbiology imeni Avgust Kirkhenshteyn of the Latvian SSR Academy of Sciences (IMB).

M. Ye. Beker, academician of the Latvian SSR Academy of Sciences, director of the Latvbiotekhnologiya Republic Intersectorial Scientific and Technical Complex, opened the conference. He familiarized in detail those present with the new system of organization of priority directions in scientific and technical progress in the national economy. The complex includes 22 organizations. Research work is distributed among 14 subprograms. No matter how good and advanced the obtained technological solutions may be, without their embodiment in the material, instruments, or apparatus the work will not be completed, that is, a modern real biotechnological process realized in an apparatus model—a bioreactor, a unit, a line, or a plant—should be the final result.

A. M. Bezborodov (the Institute of Biochemistry imeni A. N. Bakh of the USSR Academy of Sciences), chairman of the "Industrial Microbiology" Section of the Scientific Council for the Overall "Microbiology" Problem, noted that, despite the enlistment of a big collective of scientific workers and planners in the development and design of apparatus for conducting microbiological synthesis processes, the organization of cycle development, testing, and introduction of prototypes and pilot units was imperfect and often led to too long periods of production of new equipment.

In the opinion of *A. M. Kuznetsov,* deputy director of the Irkutsk Scientific Research and Design Institute of Chemical Machine Building, this is connected primarily with the disconnection among planning and design organizations, the industry producing fermenting equipment, and scientific workers engaged in the development and modernization of apparatus. There is no strict formulation of a technical problem and specification of technical requirements on the part of clients—sectorial and academic institutes developing biotechnological processes. It should be admitted that scientific research institutes conduct insufficiently profound research aimed at analyzing and determining key indicators of biosynthesis processes under conditions of a pilot or industrial operation, which should be taken as the basis in the course of design developments. As a rule, the models of fermenters developed by the Irkutsk Scientific Research and Design Institute of Chemical Machine Building do not receive an appropriate objective and competent evaluation by technologists and specialists in operation. A number of designs have not been used by clients according to purpose even once. Only one-half of the 75 fermenter designs have been tested on schedule and even fewer have been mastered by machine building plants producing series equipment for outfitting newly built microbiological industry plants. Production tests of already developed and manufactured models have been dragging out for an intolerably long time.

V. V. Biryukov (the Moscow Institute of Chemical Machine Building) discussed the requirements placed on the technological and apparatus formulation of processes connected with the biosynthesis of secondary metabolites, primarily antibiotics. Basically, the problems are the same as at the Irkutsk Scientific Research Institute of Chemical Machine Building—the lack of clear specifications on the part of clients, that is, sectorial and academic institutes developing new biotechnological processes, which hampers the implementation of an optimal design development. For example, the fermenter design and cultivation regime affect not only the consumed capacity, average gas content, and reduced air speed, which is indisputable, but, it turns out, also the characteristics of distribution of individual phases, asepsis of cultivation conditions, metabolism of microorganisms, and so forth.

A number of reports were devoted to theoretical computations for individual subsectors of production of fodder yeast on wood hydrolyzates (*V. N. Sokolov,* the Leningrad Technological Institute imeni Lensovet), baker's yeast (*M. P. Gandzyuk,* the Kiev Technological Institute of the Food Industry), lysine (*V. V. Krikis,* IMB), and yeast on normal alkanes (*A. Yu. Binarov,* the All-Union Scientific Research Institute of Protein Synthesis). The latter noted a number of shortcomings in the operated bioreactors of the ADR-76-900 series and substantiated the advisability for their modernization for the production of gaprin, that is, yeast on normal paraffins. The final design of a fermenter for an industrial production of gaprin has not yet been selected. However, preference should be given to bioreactors with a jet type of circulation of the culture liquid and saturation of the medium with oxygen and natural gas.

Energy-saving fermenters, owing to their design features, are promising precisely for the cultivation of bacteria of the *Brevibacterium* genus—producers of irreplaceable L-lysine aminoacid, whose annual production totals

20,000 tons in the USSR now. However, the real need exceeds this amount fivefold. With a comparatively simple solution—a successive connection of three fermenters, each of which had a capacity of 100 cubic meters, supplied with contact devices in the form of perforated plates it was possible to increase the available operating capacity of fermenters (*V. V. Krikis*). This study was performed under the guidance of U. E. Viyesiur, academician of the Latvian SSE Academy of Sciences.

This report differed from the general opinion to the effect that the path of unification of equipment should be followed in the future. Nevertheless, IMB bioengineers demonstrate the need for the development of special designs for every culture or production process. *M. A. Rikmanis* recommended the use of a fermenter with counterflows of the mixed medium for mycelial cultures, which made it possible to shorten in one-half the time of cultivation of trichodermin—a preparation for the protection and stimulation of the growth of vegetable crops (A. F. Apsite).

The reports by *V. S. Andreyev et al.* (the All-Union Institute of Highly Pure Biopreparations and the Special Design Office of Fine Biological Machine Building of the Ministry of the Medical and Biological Industry), *G. V. Kotelnikov* (the Special Design Office of Biological Instrument Making of the USSR Academy of Sciences), and *M. Zh. Kristapson* (IMB) were devoted to laboratory and pilot units. Positive experience in the development of small-scale fermenting equipment has been accumulated in the country, but there are no production capacities, which would ensure the ever growing needs of scientific organizations and plant laboratories. Moreover, the poor cooperation in the development of laboratory equipment among the organizations of the USSR Academy of Sciences, the Union republics, and the USSR Ministry of the Medical and Biological Industry should be noted.

A. I. Kestner (the Tallinn Polytechnical Institute) reported on the apparatus formulation of the biotechnological process with the application of immobilized biocatalysts, including enzymes and cells. In a certain approximation this process can be considered the process of the future. However, in order to implement it in practice, it is necessary to carry out large-scale bioengineering work.

In their resolution the participants in the conference expressed confidence that a fermenter of the future designed for a long-term period would be developed and the problem of coordinating bioengineering operations of numerous organizations and groups would be solved and also recommended that the specialty "bioengineering" be singled out in higher educational institutions (on the basis of specialties 0516 and 0517 "machines and apparatus of microbiological production") and so forth.

The participants in the conference were given the opportunity to become familiar at the IMB with existing fermenting units of domestic (ANKUM-2, FU-8, FU-30, and so forth) and foreign production (for example, the foreign firms MBR, New Brunswick, LKB, and so forth), as well as at the institute's bioengineering laboratory, with an automated fermenting system containing three FS-6 bioreactors of a capacity of 5 liters each and the Biotron-M microprocessor complex, which includes an Elektronika-60 microcomputer, a Mibarm console on KTS LIUS-2 plates, a seven-color display with a Dialog keyboard, and an alphanumeric printer. The "computer-fermenter" complex makes it possible to identify under real conditions various mathematical models uncovering the interaction between external conditions and the metabolism of microorganisms, as well as to simulate various design features of the apparatus.

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